ack^d to Dr. Primrose.

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TRANSACTIONS

OF THE

CONGRESS

OF

American Physicians and Surgeons

SEMI-CENTENARY
SIXTEENTH SESSION

HELD AT

ATLANTIC CITY, N. J.

May 3rd and 4th, 1938

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OF
1938

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BY-LAWS OF THE CONGRESS

OF

AMERICAN PHYSICIANS AND SURGEONS

1.

This organization shall be known as the

CONGRESS OF AMERICAN PHYSICIANS AND SURGEONS.

2.

It shall be composed of national associations for the promotion of medical and allied sciences.

3.

It shall hold its sessions at 5 year intervals.

4.

The officers of the Congress shall be a PRESIDENT, VICE-PRESIDENTS, A SECRETARY, A TREASURER, AND AN EXECUTIVE COMMITTEE.

5.

The PRESIDENT shall be elected by the Executive Committee, of which he shall be *ex-officio* a member. He shall preside at the sessions of the Congress. He shall deliver an address.

6.

The PRESIDENTS of the participating societies shall be *ex-officio* the VICE-PRESIDENTS of the Congress.

7.

The SECRETARY and the TREASURER shall be elected by the Executive Committee. They shall be *ex-officio* members of the Executive Committee.

8.

The EXECUTIVE COMMITTEE shall be composed of one (1) member from each participating Society and said members shall be elected by the various Societies at the next annual meeting subsequent to the Congress.

It shall be charged with all duties pertaining to the organization of and preparation for the ensuing Congress, including the election of all officers and of a Committee of Arrangements.

9.

The expenses of the Congress shall be divided between the participating Societies in proportion to their membership.

10.

The admission of new associations to participate in the Congress shall be by unanimous vote of the EXECUTIVE COMMITTEE.

MINUTES

A meeting of the Executive Committee of the Sixteenth Congress of American Physicians and Surgeons, for 1938, to which the Presidents and Secretaries of the component societies were invited, was called after the President's dinner at Haddon Hall, Atlantic City, on the evening of May 2nd, 1938.

Those present were:

Dr. Thomas J. Harris, representing American Otological Society

Dr. Daniel J. McCarthy and Dr. James B. Ayer, representing American Neurological Association

Dr. Guy L. Hunner, representing American Gynecological Society

Dr. James H. Mitchell and Dr. Otto H. Foerster, representing American Dermatological Association

Dr. William Darrach, representing American Surgical Association

Dr. Thomas Darlington, Dr. G. Morris Piersol, and Dr. Francis M. Rackemann, representing American Clinical and Climatological Association

Dr. O. H. Perry Pepper, representing Association of American Physicians

Dr. Francis R. Hagner, representing American Association of Genito-Urinary Surgeons

Dr. Frederick C. Kidner, Dr. J. T. Rugh, and Dr. Ralph K. Ghormley, representing American Orthopedic Association

Dr. Howard C. Carpenter and Dr. Hugh McCulloch, representing American Pediatric Society

Dr. Ward J. MacNeal, representing American Association of Pathologists and Bacteriologists

Dr. James B. Herrick, President

Dr. John T. King, Secretary

Minutes of last meeting and Treasurer's Report were read and approved.

Various matters of business were brought to the attention of the group by the Secretary. It was voted unanimously to lay all these matters on the table as being without the province of the Congress. However, a resolution was adopted in answer to a request for support from the California Society for the Promotion of Medical Research in its fight against the proposed State Hu-

mane Pound Law. The following resolution, proposed by Dr. O. H. Perry Pepper, seconded by Dr. Thomas Darlington, was unanimously carried: "That the Executive Committee of the Congress is opposed to any legislation which limits the advance of medical science through properly conducted animal experimentation."

A letter from Dr. Weidman, Secretary of the American Dermatological Association, in which he explained the reasons for the absence of his Association from Atlantic City, was read. The Secretary was instructed on the motion of Dr. Darlington, seconded by Dr. Hagner, and unanimously carried, to write an appropriate letter to the Dermatological Association regarding its absence from the Congress meetings.

Attention was then directed to the proposals of Dr. Daniel J. McCarthy, transmitted through the American Neurological Association. After vigorous discussion the following motion was put by Dr. McCarthy, seconded by Dr. MacNeal, and carried unanimously: "That the President appoint a Committee of five from among those present at the meeting; that each constituent society be invited to appoint three delegates to meet with those selected by the President; that this joint Committee be called together by the Secretary; and that its purpose shall be consideration of reorganization of the Congress." The following five from among those present at the Atlantic City meeting were named by Dr. Herrick as the nucleus of the proposed Committee:

Dr. John T. King, Chairman
Dr. Thomas J. Harris
Dr. Daniel J. McCarthy
Dr. O. H. Perry Pepper
Dr. Francis M. Rackemann

The meeting was then adjourned.

On the evening of Tuesday, May 3rd, the President, Dr. James B. Herrick, who was introduced by Dr. Esmond R. Long, gave his address on "Some Features of Present-Day Diagnosis." Approximately 500–600 persons attended this address and the Reception which followed.

On the following afternoon, May 4th, the general scientific session was held. The Secretary first read the resolution of the

Executive Committee relative to the proposed California State Humane Pound Law, and asked for an expression of opinion. On the motion of Dr. James Paullin, duly seconded, the President declared the action of the Executive Committee unanimously supported.

Next, the Congress voted without dissent to instruct the Secretary to write letters in support of the Bills now before the Congress of the United States to improve the facilities of the Army Medical Museum.

The scientific papers were then delivered, according to the program.

GUESTS OF THE CONGRESS

By Invitation of the Executive Committee

The Surgeons-General of the Army, Navy, and Public Health Service of the United States.

REPORT OF TREASURER
16TH CONGRESS

Congress of American Physicians & Surgeons

RECEIPTS

March 28, 1938, Balance on hand in American Security & Trust Co.	$1749.65	
Registration fees received for 16th Congress (386)	1930.00	
One extra copy of Transactions	1.15	
Total Receipts	$3680.80	$3680.80

DISBURSEMENTS

Printing receipt books & envelopes (Eynon Print Co.)	$ 12.72	
Bank charge on five Canadian checks	.45	
Woodington Mail Advertising Co. (Notices, etc., for Dr. Rugh)	173.59	
Postage for Treasurer	10.00	
Printing extra receipt books (Eynon Print Co.)	8.75	
Printing programs (John H. Saumenig & Co.)	442.25	
Miscellaneous expense (telephone, telegrams, etc.) for Treasurer	5.00	
Clerical work for Treasurer	75.00	
Chalfonte-Haddon Hall (Reception; Orchestra; Meeting hall)	240.00	
Dr. Herrick (expense for meeting of Presidents & Secretaries of affiliated societies at Atlantic City)	15.00	
Master Reporting Co. (Reporting at Congress)	17.86	
Miscellaneous expense in preparation for Congress (Dr. King)	56.45	
Clerical work for Doctor King	60.00	
Stationery for Dr. King (John H. Saumenig & Co.)	9.75	
Transactions (printing and publication) (Postage not included)	625.70	
Total Disbursements	$1752.55	$1752.55
October 19, 1938, balance on hand in American Security & Trust Co.		$1928.25

Francis R. Hagner, M.D., *Treasurer,*
Congress of American Physicians & Surgeons

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Members present are indicated by.*

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Organized 1866

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Organized June, 1875

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Organized June, 1878

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Dr. William H. Watters,	Boston, Mass.
Dr. Theodore R. Waugh,	Montreal, Canada.
Dr. Leslie T. Webster,	New York, N.Y.
Dr. Lewis H. Weed,	Baltimore, Md.
*Dr. Grover C. Weil,	Pittsburgh, Pa.
Dr. Herman G. Weiskotten,	Syracuse, N.Y.
Dr. Emil Weiss,	Chicago, Ill.
*Dr. Carl V. Weller,	Ann Arbor, Mich.
Dr. H. Gideon Wells,	Chicago, Ill.
Dr. Paul G. Weston,	Jamestown, N.Y.
Dr. Mary W. Wheeler,	Albany, N.Y.
Dr. George H. Whipple,	Rochester, N.Y.
Dr. Courtland Y. White,	Philadelphia, Pa.
Dr. Ellen P. Corson White,	Philadelphia, Pa.
Dr. Eugene R. Whitmore,	Washington, D.C.
Dr. Frederick W. Wiglesworth,	Montreal, Canada.
Dr. Ray Lyman Wilbur,	Stanford University, Calif.
Dr. Sigmund L. Wilens,	New York, N.Y.
Dr. Herbert U. Williams,	Buffalo, N.Y.
Dr. John W. Williams,	Cambridge, Mass.
Dr. Henry S. Willis,	Northville, Mich.
Dr. Charles K. Winne, Jr.,	Albany, N.Y.
Dr. Milton C. Winternitz,	New Haven, Conn.
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Dr. Nathan A. Womack,	St. Louis, Mo.
Dr. David A. Wood,	San Francisco, Calif.
Dr. Francis C. Wood,	New York, N.Y.
Dr. Charles E. Woodruff,	Northville, Mich.

Dr. Angus Wright,	Rochester, N.Y.
Dr. Arthur W. Wright,	Albany, N.Y.
Dr. Krikor Y. Yardumian,	Pittsburgh, Pa.
Dr. Isolde T. Zeckwer,	Philadelphia, Pa.
Dr. H. M. Zimmerman,	New Haven, Conn.
Dr. Hans Zinsser,	Boston, Mass.

RECAPITULATION

	Emeritus, Senior, Active and Associate	Corresponding	Honorary	Present
American Otological Society	136	..	10	3
American Neurological Association	234	..	25	30
American Gynecological Society	88	..	40	1
American Dermatological Association	129	24	8	2
American Laryngological Association	118	18	3	6
American Surgical Association	248	..	14	50
American Clinical and Climatological Association	213	..	20	83
Association of American Physicians	307	1	10	107
American Association of Genito-Urinary Surgeons	89	9	7	25
American Orthopedic Association	160	23	5	33
American Pediatric Society	127	2	15	7
American Association of Pathologists and Bacteriologists	564	..	..	77
	2413	77	157	424
Total Membership of Congress		2647		
Guests and Visitors				41
Total Attendance				465

THE PRESIDENT'S ADDRESS

CONGRESS OF AMERICAN PHYSICIANS AND SURGEONS

INTRODUCTION OF DR. HERRICK

ESMOND R. LONG, M.D.
Philadelphia, Penna.

MEMBERS OF THE CONGRESS OF AMERICAN PHYSICIANS AND SURGEONS, LADIES AND GENTLEMEN:

In the slow rotation of seniority in the component societies of this Congress it is this year the pleasant task of the representative of the American Association of Pathologists and Bacteriologists, as Senior Vice-President, to introduce the President of the Congress.

It will be quite unnecessary for me to tell you much about Dr. Herrick. Many of you are fortunate enough to be acquainted with him personally and all of you know him as a distinguished figure in modern American medicine, notable for his contributions in the field of coronary artery and heart disease, the discoverer of sickle cell anemia, for years Chairman of the Department of Medicine of Rush Medical College, and a former President of a constituent body of this Congress, the Association of American Physicians.

I could not fail, however, at least to call attention to his distinction in scholarship. He is recognized as a valuable contributor to medical history,—and to note his interest in classical literature I need only recall his famous address before the Association of American Physicians on "Why I Read Chaucer at Seventy."

Above all, however, I would like to pay tribute to the rare charm of his personality. Few men that I ever knew have so commanded the affection of their friends and students. And here may I speak, quite simply, as one of those students. I hope you will pardon a personal reminiscence. Like many in this room I had the good fortune to be a pupil of Dr. Herrick, in his heart clinic, in the top-floor amphitheater of the old building of Rush Medical College. In those days when an instructor closed his last clinic it

was customary for the students to applaud. The tribute was often routine, and not without an eye to the forthcoming examination. When Dr. Herrick ended his last clinical demonstration, however, there was a tremendous burst of applause of indubitable spontaneity. He bowed in his gracious way, left the amphitheater and walked down the six flights of stairs to the street. The students continued clapping. They were still applauding long after he must have left the building. He could not possibly hear them, but the students wanted somebody, each other perhaps, to know how much they thought of the man. I tell this simple story because I am sure the members of this Congress have quite the same warm regard for him. Ladies and Gentlemen, Dr. Herrick.

SOME FEATURES OF PRESENT-DAY DIAGNOSIS

JAMES B. HERRICK, M.D.
Chicago, Ill.

To have been elected President of the Congress of American Physicians and Surgeons is an honor that is highly appreciated and for which sincere thanks are here tendered. The distinguished men who in the fifty years of its existence have held this position, almost without exception in their presidential addresses discussed topics concerning which they had first-hand knowledge derived from personal experience. In conformity with this wise precedent, I shall speak tonight from the viewpoint of a clinician whose fifty years as medical practitioner and teacher have been intimately and chiefly concerned with the patient. I shall confine my remarks to one phase only of clinical medicine, viz., diagnosis and some of its present-day problems.

Can anything new be said concerning diagnosis? Have not its principles and its methods been firmly established for centuries? Cannot one predict that for generations to come physicians will still be trying to answer the question, "What is the matter with the patient" by following the time-honored procedure of considering the hereditary, environmental and personal history; the story of the present complaint; the physical examination; the reports of laboratory; instrumental and therapeutic tests; the

advice of specialists; finally, the assembling of all these facts, their careful analytic and synthetic study, and their summation in a logical conclusion?

Why, then, bring up a subject so trite?

I might plead the necessity of repeating the wellknown from time to time lest it be forgotten; also, the importance of the topic, for the desire to make a correct diagnosis by which the way is prepared for rational treatment is the most compelling motive in the practice of medicine. A more potent reason, however, is that diagnosis today presents problems that are quite different from those of even a decade ago, for diagnosis is not as stable as it is often thought to be. The order of procedure may remain the same but technic changes. Every addition to medical knowledge carries with it the necessity of a revision of the methods of diagnosis. The microscope, bacteriology, x-ray, applied chemistry, endocrinology, these and many other factors have combined to make diagnosis far different from what it was when it was chiefly a matter of scholastic musing, adherence to tradition, and idolatrous veneration of the fathers of medicine. These newer facts in medicine and cognate sciences, facts that aggregate a huge mass, have in some respects rendered diagnosis simpler and more accurate; in other respects, more difficult and more complicated.

At present, diagnosis, as well as medicine in general, is in a good deal of turmoil, with many problems pressing for solution. These will not be solved, though the solution may be helped, by resolutions or pronouncements of medical organizations, reports of special committees, or recommendations of foundations of various kinds, no matter how sincere and searching the efforts of any or all of these bodies may be. They will not be solved by the utterance of epigrams like "train for power," "back to Hippocrates," "back to Galen," for like most wise sayings, these are but partial truths. The answers will not be found by cloistered meditation in the library, nor by mere sitting in at a pedagogic conference, nor by indulging in day dreams in which the ideal and even the idyllic are permitted to becloud reality. Diagnosis is an eminently practical process, concerned with human beings; with pain and bleeding, with germs and fever, with failing function of organs, with threatening death. Theory and science are involved, of course. But diagnosis implies the application of theory and science. As electrical engineering needed an Edison as well as

a Faraday, so modern medicine is a debtor to Lister as well as to Pasteur.

The solution will come mainly through evolution, by the process of trial and error based on the experience of general and special practitioners, research workers in ward and laboratory and on the reaction of the public, i.e., the patients themselves,—and the patient, let it be noted, is the party whose interests are paramount. All these other agencies that I have mentioned may be helpful, though not decisively final. A frank statement of difficulties, with tentative suggestions for remedies, may also be helpful, though also indecisive. It is in such a hope that, repeating much that has been said by others as well as by myself, I venture to discuss here some—by no means all—features of modern diagnosis. By speaking often in the first person singular it will be evident, I trust, that I am not presuming to express in this address any but my own opinions.

A prolific cause of errors in diagnosis is ignorance, varying in degree of course, on the part of the practitioner. He may be lacking in information because he has no urge to study, has never been taught to study, or perhaps lacks the ability to study. He made a mistake in his choice of a profession; the medical school erred in encouraging him or even permitting him to be a physician. He fails to keep abreast of the times by reading and by conferences with his colleagues. He loses touch with the laboratory and the morgue. He is either a forceless, inefficient man who, feeling his inferiority, attempts but little and does that poorly; or he may be one who, possessing only the little knowledge that is a dangerous thing, becomes a menace because he is blissfully unaware of the meagerness of his knowledge. Where better informed and wiser men would fear to tread, he rushes in with scalpel or harmful drug or half-baked theory, before he knows the real nature of the ailment he has been called to treat.

The threat from this type of doctor who is unaware of his limitations is one of the strongest arguments for intensive work in undergraduate and intern days, e.g., the exhaustive study of a case or a group of cases through ward, laboratory, operating room, perhaps the dead house. Or it may be a problem studied in some department, such as pathology or physiology. Such work will inculcate the principle of thoroughness, the importance of reading original articles and monographs and not merely textbooks. By

such intensive work the student learns how medical knowledge is acquired and what are its present-day deficiencies. He is better able to distinguish between theory and fact; he gets rid of the incubus of unthinking veneration for the printed word. He learns to reason and judge for himself, though the responsibility for training in independent thinking should not fall primarily upon the faculty of the medical school but rather upon the school of arts and sciences, a point dwelt upon in 1900 by H. P. Bowditch in his presidential address before the Fifth Session of this Congress.

This "majoring" in the medical school has been opposed by some who in their fetish-like worship of the old type of general practitioner, not realizing, or ignoring, the tremendous changes that have taken place, argue that the student should not be permitted to do any intensive work because it smacks of specialism. To these objectors specialism is anathema. Is it not time that this out-moded attitude be given up?

The principle of majoring should be carried over into the life of practice. Unless this is done, the practitioner goes stale. Concentration on some subject with the accompanying sense of mastery and the resultant zeal for the new, is what will save doctors from remaining mere drudges, with no pleasure in their daily grind, with no sense of progress. This is not specialism in the strict sense. It is expertness, superior knowledge and skill. The process is not a narrowing one; on the contrary, it is broadening.

There is another advantage that will come from this intensive study. It will make clear to the doctor that he has not performed his whole duty when he puts the proper caption on a disease. He should know the cause of such disease in general, and the manner in which such cause has operated in the particular case in hand. He should be familiar with the alterations in anatomy and physiology that are involved, should have knowledge of the natural course of the disease, the best way of handling it, the dangers to the patient and to others, the social and economic import of the illness. This implies well directed instruction on the part of the teacher; much observation and wisely utilized experience on the part of the practitioner.

But it is impossible for even the diligent and bright doctor to know all. There is too much of it. He must select certain topics towards the mastery of which his major efforts are directed. The medical school may, perhaps should, offer him the opportunity of

choosing from a wealth of courses. It should guide him in selecting what seems most suitable to him as an individual. It should *compel* him to select what is essential to physicians as a class, that which teaches the broader, fundamental principles and the facts that are necessary for his everyday work as a practitioner and for his future development. All this is no easy task. The problem of what constitutes wise guidance for the undergraduate, postgraduate, and graduate student is being given careful, expert consideration by practitioners themselves, by medical schools, by able committees of investigation and by such bodies as the Council on Education and Hospitals of the American Medical Association that has functioned so long and so well. Much progress has already been made.

It may be added here that many of us who are older magnify the difficulty that the undergraduate or young practitioner has in grasping even a respectable fraction of the huge mass of knowledge that has accumulated in the last fifty years. We recall the struggle we had when, bewildered, we tried to understand the new that was then in the chaos of formation. We forget that many questions that were at that time subjects for argument and investigation are now settled. The tenets of bacteriology are approved, aseptic surgery and midwifery are established practices, the morphologic and chemical examination of the blood, the x-ray are accepted as helpful aids. Students of today have similar though different problems to face but the difficulty of learning much that we struggled with is not as forbidding as we often think.

Ideally the doctor should be able by himself to interview and examine his patient, make the instrumental and laboratory tests and reach a decision as to diagnosis. This ideal is rarely realizable, for our doctor, even though a paragon, cannot do these things unaided. How can he best get help? Physicians are already answering this question by methods determined by individual needs, opportunities and experience. One takes an assistant or associate. Another joins colleagues in hiring and supervising a competent technician, or he becomes a member of a group or clinic that may include specialists of several types; or he avails himself of the services of his hospital, the municipal laboratory, or a properly conducted private laboratory.

Yet these plans have certain weak features. The further away

the doctor is from the laboratory, the instrument, the consultant, and most important of all from the patient, the greater is the likelihood of error. The doctor by eliciting the history himself may learn as much from the way a patient answers questions as from the answers themselves. If the doctor sees for himself the x-ray film, the stained blood under the microscope, he has a more nearly correct impression than that conveyed by merely reading the report of the consultant or assistant. Also many instruments and special tests are not as precise as they are sometimes thought to be; the technician is prone to error in interpreting what he sees in the laboratory just as is the doctor when he tries to translate into pathology what he observes at the bedside. And there is a real danger from overspecialization. These topics have, however, been so frequently and so well discussed that to take them up further in this paper would be needless repetition. From the standpoint of diagnosis, nay, from that of medical practice in a broader sense, may we not accept the specialist, the laboratory, and some forms of group practice as *faits accomplis?* But first, the specialist, the laboratory, the group must show by certification or some other test that they are *worthy* to offer reliable aid to the practitioner.

There is another feature of modern diagnosis, of minor value perhaps, that is worth consideration. Not all patients need the thorough going over that they are often given. The family doctor is familiar with the past health history of his patient. His problem is that of the present illness. With a few questions, a snappy physical examination, he recognizes an erysipelas or measles or an acute cardiac failure. He may use the thermometer, the blood counter or the rubber glove but he sees no call for the Wassermann test, for the x-ray film or the electrocardiogram. He is well aware that everyday symptoms that seem simple may be due to disease that is serious. Headache may mean tumor, rapid pulse may be due to perverted thyroid action, dizziness may come from pernicious anemia, the acute indigestion may mean appendicitis, carcinoma of the bowel or coronary thrombosis. But, he feels that many patients with stomach and bowel upsets, for example, and other everyday ailments with no urgency about them are quite properly examined and treated for a time on the basis of a provisional diagnosis. They need not be rushed to the hospital for study of stools, tonsils, teeth, sinuses, blood chemistry and the like. He agrees with Mackenzie that when one wishes a flat tire fixed, one resents

the advice of the garage man that a thorough overhauling of the car is necessary. It is here that there comes into play not alone the knowledge possessed by the physician, but also his discriminating good sense and his mental acumen kept sharp by experience. He will realize that when life may be urgently threatened by waiting, the safety of the patient must incline the decision to immediate action. "To be informed is to avoid dangerous errors in practice," said Billroth. Knowledge and above all else wisdom are here at a premium.[1]

I wish to utter a word of caution as to the way in which diagnoses are sometimes made in connection with the periodic examinations or health check-ups that are so popular today. In cases with obscure symptoms that possibly portend evil, each and every form of examination may be indicated. So, too, there can be no quarrel with the doctor who feels that he can earn an honest dollar if he yields to the demand of his intelligent patient that, regardless of time or expense, a complete examination be made and a detailed opinion be rendered as to the state of health. Yet even here caution is necessary. Some investigations, e.g., bronchoscopies, ureteral catheterizations, exploratory punctures, allergic tests, are not entirely devoid of risk. Nor is it always wise to discuss with an already apprehensive patient symptoms that are trivial and negligible. Anxiety neuroses and phobias are easily aroused. Such mental upsets can be avoided if the doctor understands patients as well as disease and has the ability to convey truthful information in a way that does not terrorize. Fortunately, too, some patients are well poised and not easily disturbed mentally. A lady of fifty asked my opinion of the report of twenty-five pages that had been handed her as the result of a study of her case in a reputable clinic. Fourteen diseased conditions had been found and

[1] The same tendency to advise unnecessary examination is seen in the office work of general practitioners, specialists and in the group or clinic. Examination by x-ray, electrocardiograph, by Wassermann or metabolism test would rarely add usable knowledge in the case of a patient with a rheumatic mitral stenosis and a moderate degree of congestive heart failure. On the other hand, a patient with a leaky aortic valve and threatening heart failure may present an entirely different problem. The cause of the lesion—rheumatism, syphilis, arteriosclerosis, hypertension—the possibility of aneurysm or even of an error in diagnosis with a congenital defect or a coarctation of the aorta causing the symptoms, may make one or several of these tests imperative. Proper therapy may depend upon their results.

were duly listed. As I finished reading, I said, "Well, what did you think about it all?" "Doctor," she replied, "if there had been two or three conditions reported it would have scared me stiff. But when I saw fourteen I just laughed." A pretty sensible view to take of some of these reports.

To tell a patient what ails him requires much understanding of human nature and much tact. One should be careful not to alarm unduly nor to convey a wrong impression. Emerson has said, "It is not the fact that imports but the effect or the impression of the fact on the mind." To tell a patient that he has a leaky heart valve or syphilis or diabetes may be to state a fact. If the effect of this unexplained statement is to convey to the layman that he has a disease that is hopeless, that will progress relentlessly to an early fatal issue when such is not the case, one has by stating a fact conveyed a wrong impression; has told an untruth. One must adapt the statement to the intelligence of the hearer and by explanation and qualification make it convey the truth that is necessary for the proper understanding of the condition and the carrying out of the advice that is to be given.

Many other features of diagnosis that present minor problems might be discussed did time permit and were it profitable to dwell on what would be agreed to without argument. Among these may be mentioned the importance of having no preconceived notion as to what is the matter when one tackles a case of illness. One should go in with an open mind, though one should not keep the mind constantly open. As G. K. Chesterton said, "The object of opening the mind as of opening the mouth is to shut it again on something solid."

Then there is the doctor whom we all know who lets his diagnosis depend too much upon his pet symptoms. A peculiar lustre to the eye, a tint of the skin or a special brand of cough or of pain and the doctor's mind is, if not already made up, at least strongly prejudiced. There is the bluff doctor who breezes in and with a rough and ready air, after a cursory examination, makes a cocksure diagnosis that may turn out to be correct. His more scholarly and scientific colleague sarcastically comments that this doctor doesn't know enough to hesitate or be in doubt.

One might discuss the diagnosis by exclusion; or the problem presented when two or more diseases are present rather than one; or the importance of revision of a diagnosis. One might consider

further than has been done the perils from emphasizing one of the diagnostic procedures at the expense of others. "Doctor," said a patient to me, "I hope you will be different from the many physicians whom I have consulted. I hope you will examine the x-ray films less and me more." There is a good text for a sermon: in examining the films do not overlook the patient.

There is one feature concerning which I wish to speak a little more at length. To state it paradoxically, some physicians know too much to be good diagnosticians or safe advisers. They have more knowledge than they can well handle; they are "suffocated beneath a dead weight of erudition." A doctor of this type knows a multitude of facts. But these facts and their arrangement in the doctor's mind resemble the motley collection seen on the medicine shelves of the bathroom. To be of value, facts, whether they are the result of planned research or of accumulated experience, must be seen not in their isolation but in their relation to other facts. President Neilson of Smith College expressed it the other day when he said that "truth lies not in facts but in the relations between facts." The physician or surgeon may lack the ability to distinguish between major and minor symptoms of disease. He fails to realize that there are what might be called the non-essentials of diagnosis. One of these non-essentials held too close to the eye may obscure the central field of vision and the essentials may not be seen. He may be so over-conscientious as to be timid, so obsessed by the laudable desire to be thorough that he putters over minutiae and overlooks the obvious. Valuable time may be lost in waiting for the blood count, the icteric index, the electrocardiogram, the x-ray film, and the golden—perhaps the arsenical—opportunity for prompt action slips by, the favorable time for operation, for giving antitoxin, or prescribing bed rest, is lost.

There is such a thing as being too particular.[2] We may apply to medicine what Mr. Justice Cardozo says about the law: "There is an accuracy that defeats itself by over-emphais of details." At times this unfortunate stressing of the incidental is a defense reaction, a desire to appear judicially minded and to reach no conclusion until all the evidence is in. Again, following Justice Cardozo,

[2] Bichat expressed it when he said there were two perils equally to be feared: that of particularizing too much and that of generalizing too much. The second, he said, leads as well as the first to false results. (Quoted by Bouillaud, Traité des Maladies du Coeur, p. 254.)

this is an invertebrate habit of mind which thinks it is impartial because it is undecided and which regards the judicial attitude as that which refrains from judging.

To what extent should the doctor seek for these less common or even out-of-the-way signs? How can he assess them at their proper value? Should they be taught to the undergraduate? It is not easy to give a categorical yes or no answer to these questions. As the children say: why, that depends.

The answer will depend much upon the purpose for which the diagnostic study is made. If research is the prime object, phenomena apparently the most trivial may profitably be sought and recorded in minutest detail. No preconceived notion as to their insignificance should exclude their consideration. The results may show they are of great worth. The same is true if the doctor is trying in every way to perfect himself—as he should—as a keen observer and skilled diagnostician. He should learn their value by trial. If, however, the object of the examination is to decide promptly what is the matter with the one particular individual who is before him so that this individual may be treated rationally and without delay, many symptoms may be virtually ignored to be considered only if help is needed to remove a lingering doubt. A too meticulous concern with the finer points of diagnosis may easily lead good clinicians to lose their sense of proportion and perspective.

It would be helpful if symptoms might be classified from pathognomonic or positive—tubercle bacilli in the sputum or urine, crepitus and displacement in fractured bones, shadows like those of gallstones in the film—down to those only rarely present or of lesser value. Extreme caution is here necessary. Even bone crepitus may be simulated by conditions other than fracture; the shadow confidently regarded as due to gallstones may be cast by a calcified gland. And symptoms low down in the scale may at times assume increased importance. For minor symptoms are by no means to be scorned. Take the case of pulmonary tuberculosis. The diagnosis is regarded as certain if the bacillus is found in the sputum. The x-ray film is a second major reliance. No further symptoms are necessary for a positive diagnosis. Yet in cases in which the x-ray revelations are doubtful and in which no tubercle bacilli are found, other symptoms are by no means negligible—cough, râles, emaciation, anemia, fever, rapid pulse. And such

symptoms may be of importance from another point of view. They may enable one to estimate the gravity of the illness more definitely than is possible by the x-ray or the study of the sputum, for the number of bacilli or the extent of the diseased area as revealed by x-ray do not always declare the seriousness. Such symptoms, therefore, should be discussed before students and considered at the bedside.

An extreme view of this aspect of the non-essentials that I have presented is taken by some who say that undergraduates should not be taught the unusual, the less important or the imperfectly understood in diagnosis. Why, they say, should the practical man at the bedside be concerned with systolic apical murmurs? They generally mean little and are often misinterpreted. Why should he bother about slight variations in blood pressure, poorly understood features of x-ray films? Diagnosis based on fundamentals and essentials is "good enough" for the ordinary doctor.

This extreme view seems to me a mistaken one. As I have said, the dangerous doctor is the mediocre man who is unaware of his own limitations and the pitfalls of practice and does not know the unusual when he meets it. The most reliable man is he who knows the most and knows his own ability and his limitations.

Another reason why one may object to this "good enough for the ordinary doctor" attitude is that, while apical systolic murmurs—to use this as an example—often have no sinister meaning, sometimes they mean much. Because physicians frequently misinterpret is not a valid reason for ignoring the murmur or for discarding the stethoscope and all it stands for. It is rather an indictment of the profession in general for lack of accurate knowledge concerning this murmur. Is it not the duty of the schools and the leaders in medicine themselves to learn more about such things and to teach more efficiently?

The wisdom of the policy of teaching in the undergraduate courses only the essentials of medicine is debatable for another reason. By compulsory education in our public schools all children may be taught to read and to write a legible hand. The standard of the mass is thus raised. But the child so taught does not necessarily become an educated man in the higher sense of that term, nor an author, nor even a discriminating judge of good literature. This has been pointed out by an acute observer, Professor Wilbur Abbott, who shows how popular education may lower the stand-

ards of the best writers. For these writers unconsciously or consciously are led to write down to the level of the reading public, now become so enormous in number, with which is the market for their wares. Many of the histories and biographies of the day, best sellers by virtue of attractive style and the atmosphere of romance are yet lacking in the elements that should, and formerly did, mark truthful, scientific history and biography. In a similar manner may not the plan of educating doctors only in the essentials, the three R's of medicine, involve a lowering of the standard for the mass of doctors? May not this in turn drag to a lower level the superior man, the specialist, the investigator?

Then, what seems to me an unfortunte attitude has been taken by some who say that there should be a sharp line of demarcation between the ordinary practicing physician, whose duty is to do the daily grind of telling what is the matter with and treating the patient, and a higher type of scientific clinician whose function is investigation. Sir Thomas Lewis, who so richly deserves the distinguished medal for his research service to medicine and whose opinion on problems of practice cannot be lightly brushed aside, favors this distinction. The one type of doctor would be concerned with what he calls "curative medicine" ministering to the immediate needs of sick individuals, and the other with progressive medicine or "clinical science." The latter group would search for new facts, the former would simply apply knowledge already known.

I agree with nearly all that Sir Thomas says in his stimulating paper of eight years ago.[3] But it seems to me that there is an implied slur on the aims and abilities of the general practitioner that should not go unchallenged. There are many poor practitioners, one has to admit. But is it fair to judge all practitioners by the poorest, even though they be many? Not all practitioners, not even a majority of them, are of mediocre ability; not all are merely commercial in their aims; not all make their diagnoses by "no process of mental reasoning," but by a sort of glorified intuition derived from their experience as craftsmen in the art of guessing, *ars conjecturalis* to use the expression of Celsus; not all drop their contact with the laboratory and lose the spirit of research as soon as they are graduated. There can be no objection to the plan of

[3] Sir Thomas Lewis: Observations on Research in Medicine: Its Position and its Needs, Brit. Med. Jour., March 15, 1930.

intensive investigation of clinical problems by all-time qualified men in wards entirely under their control. No reproach can be cast on workers in pure laboratory research or in the most refined type of clinical investigation. All power to the small number who are qualified to carry on work of this kind, and richest opportunity! But arbitrarily to put into the class of the inferior the bright, industrious, well informed practitioner, specialist or part-time hospital physican or teacher who, imbued with the spirit of research, sees in every new and interesting case or group of cases a small problem for investigation—what is the matter with the patient, with all that diagnosis implies—seems unfair and unjust. It is discouraging to those who make up, and must of necessity for several years make up, the bone and sinew of our profession (at least in the United States and Canada) to be told that they must abandon hope who elect to enter the ranks of the general practitioner. Moreover, is it not rather extravagant to declare that little or nothing new can be expected in the future from the "curative" practitioner or specialist? That in making bedside observations he will be working in a field whose fertility is all but exhausted? That there is no prospect that any future Addison, Charcot or Skoda will add anything of value to medicine? That he must be content to do the necessary daily drudgery, that the "clinical science" investigator will do what counts? May not this view be wrong? It seems so to me.

In summing up, I realize that there are in this paper omissions and inconsistencies. Nor can I pretend to have offered completely satisfactory solutions to the problems of present-day diagnosis. The train of thought, not always connected, is that diagnosis—a process that is necessary in the everyday life of the practitioner of medicine, using the term "diagnosis" as meaning more than a perfunctory labeling of a disease—implies the application of more knowledge than any one human being can acquire, remember or properly utilize. The doctor must then have help which makes qualified laboratories and qualified specialists singly or in groups a necessity.

There has been pointed out the importance of perspective in diagnosis, the ill effects that come from being too particular regarding minute details, yet it has been contended that the practitioner must know of their existence for minute details may mean much.

Reference has been made to the unwisdom of teaching students merely the so-called essentials. It has been pointed out that such a course may make not only less efficient practitioners but may lower the morale and high standards of productive research. The value of "majoring" for the undergraduate and practitioner has been stressed.

I have expressed regret that the line of cleavage that has to be drawn—and such a line is a necessity—between the practitioner and the investigator in clinical science should be so sharply and so heavily drawn as unduly to discourage the one worker and relatively, at least, unduly to exalt the other.

It has seemed as though in the last few years there has been a tendency toward better relations between practitioners, specialists, laboratory investigators, hospitals for the care of patients, hospitals and institutes whose primary object was research, and that harmony and a spirit of cooperation have been gradually displacing the old antagonism, jealousy and misunderstanding. I fear that insistence too sharply on the separation of these two types of doctors may lead to the development of a deadening inferiority complex in the one type of worker and of a superiority complex in the other that will not improve the efficiency of either group and that in the end may have unfortunate results both in the practice of medicine as an art and in the science of medicine in the way of productive research. I endorse most heartily the plea that has been made by Soma Weiss[4] for closer relations rather than wider separation between all these groups in the belief that cooperation will be mutually beneficial.

These problems, to repeat, will be worked out largely by evolution, by trial and error at the bedside of the patient in the home and in the teaching hospitals of our medical schools. Their study by capable practitioners and educators has already helped toward clarification. All these efforts should be continued and encouraged.

Finally, unless there is now impending or shall later come upon us a second Dark Age in Science when all progress will be at a standstill, these problems never will be settled. For medical knowledge is not static; it is in a state of flux, new facts and new generalizations are constantly being established, new social and economic theories and practices are being advocated and adopted.

[4] Soma Weiss: Clinical Medicine as a University Discipline, Harvard Medical Alumni Bulletin, April 1936.

All this means there will have to be frequent readjustments. One may repeat what was said a hundred years ago by a wise clinician, Peter Latham: "Whenever in medicine anything like a discovery has been made, anything which has had the show of a principle or a law, a large surrender of cherished opinions has always followed, and knowledge has seemed to begin its career afresh from a new starting place." May I venture to predict and to express the hope that one hundred years from now medical knowledge will seem to begin its career afresh from a new starting place, for it will still be progressing.

PULMONARY TUBERCULOSIS IN YOUNG ADULTS, PARTICULARLY AMONG MEDICAL STUDENTS AND NURSES

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During the past ten or fifteen years there has been evolving a rather striking change in the concept of pulmonary tuberculosis in adults, especially in young adults.

It has long been taught that autopsy evidence adduced by Naegeli and Burkhardt, and others, indicated a well-nigh universal infection with the tubercle bacillus; that tuberculin testing beginning with Von Pirquet and widely employed for a period after 1907 confirmed the idea of general infection of city dwellers by the age of fifteen; that infection was acquired in early life (Von Behring) and that if the individual survived such infection he became allergic and was protected against ordinary or casual infection of the future; that those who developed the disease in adult life were infected from within (endogenously) by a mobilization of bacilli already in the body; that in some instances the protection conferred by an earlier infection was overwhelmed by subsequent exogenous infection. The more recently acquired knowledge alters this teaching to the extent that large numbers of individuals are now attaining adult life without having become infected with the tubercle bacillus.

Twenty years ago the value of the X-ray to discover minimal lung pathology was not generally realized and the use of tuberculin for diagnosis was languishing except as employed by the pediatrist and the veterinarian. Then began a change of view. The Framingham Demonstration was launched in December, 1916. In 1924 Massachusetts inaugurated its ten year plan to discover tuberculosis among school children by means of tuberculin and X-ray. In Oslo, Heimbeck began in 1924 his studies on nurses. Myers and different co-workers in Minnesota were beginning to glean results from the Lymanhurst School experience in Minneapolis. In 1928 Myers and Lees applied the tuberculin test to 2093 freshmen entering the University of Minnesota. Rathbun was making intensive studies of high school students and doing much to stimulate interest. In a series of papers in 1930, Myers and his

co-workers gave a summary of increasing numbers of tuberculin studies in the United States and abroad, most of them indicating a declining incidence of infection. The experience of Opie, Landis, McPhedran and Hetherington (1) in Philadelphia in their study of public school children, the results of which were published in 1929, was a notable exception. Interest in the problem of tuberculosis among school children was definitely under way.

Colleges and universities were slower in awaking. Ferguson (2) in October 1937 published a history of the movement in them. The work at Minnesota under Myers and his co-workers was the most comprehensive and their tuberculin testing of entering students in 1928 was the greatest single step forward up to that time.

By 1930 an occasional college and university were groping along. A tuberculosis committee under the Chairmanship of Dr. Ferguson was organized within the American Student Health Association at the first National Conference on College Hygiene at Syracuse in 1931. It recommended a program for tuberculosis case finding which included tuberculin testing and X-ray examination. In the summer of 1931 there was held a preliminary conference, sponsored by the National Tuberculosis Association, to consider the whole problem of tuberculosis in college students and to work out a suitable program for its solution. Since then matters have moved rather rapidly. Tuberculosis surveys have been made in over two hundred American colleges and corresponding institutions. Not all have adequate regularly operated programs. Shepard, as a result of a detailed inquiry among American colleges during 1936 and 1937, reported that fifty then had definite tuberculosis programs with regular annual examinations. The 1936–37 report of the Tuberculosis Committee of the American Student Health Association utilized tuberculin testing figures from 85 institutions.

Long and Seibert (3) published last June a summary of results with tuberculin testing among college students. For the academic year 1935–36 twenty colleges reported accurately completed tuberculin tests on 18,744 students, chiefly new entrants. Approximately two thirds of the tests were of men and one third of women. For New England and the Atlantic Coast the positives ranged from 46 to 48.9%. For the Middle-west the figures were distinctly lower, 20.6% to 31% of positives. In New Mexico there were 71 to 80% of positive reactors, presumably explained by the number of stu-

dents from families having or having had tuberculosis. Northern California and Oregon were similar to the Atlantic Coast. Southern California was slightly higher, with 50 to 60%. Reports from colleges with large groups of men and women of approximately the same average age indicated that the number of positive tuberculin tests is somewhat higher in men than in women. Where the figures for academic freshmen were kept distinct from older entering students in graduate schools the percentage of positives in the older group was higher by approximately 10 to 15%.

The seventh annual report of the Tuberculosis Committee of The American Student Health Association for the academic year 1936–37 bore upon 32,281 students the country over, all tested through the full strength of tuberculin when negative to a lesser strength. The percentage for the United States as a whole was 30.5. The figures generally were about the same as those of Long and Seibert of the previous year.

There is then satisfactory knowledge as to the amount of tuberculous infection in entering college students over the country at the present time. From less common studies it is known that the percentage increases roughly 1 to 2% per year during the college course and that the percentage of positives among men is approximately 5% higher than among women.

As to the important question of the incidence and the significance of pulmonary disease among college and university students, one is on less certain ground. There is a lack of uniformity in the interpretation of roentgenograms, in the determination as between activity and non-activity of the lesions found by X-ray, and in the methods of detection. The Tuberculosis Committee of the Amercan Student Health Association (4) recommends among other procedures routine intracutaneous tuberculin testing of entering students and a single X-ray film of all positive reactors. They further recommend a yearly film of the positive reactors, a retesting every six months of all not reacting previously, and an X-ray film when reaction is found to have changed to positive. Needless to say, there are but few institutions where such a program can be fully carried out.

Only one set of figures, that of Stiehm, (5) is included to illustrate the findings of parenchymal lesions. Of 16,101 students tested with tuberculin at the University of Wisconsin from September 1933 through February 1938, 4446 were positive. Of these positive

reactors 4215 were roentgenographed. Of the 4215 roentgenographed, 188 showed parenchymal lesions. Of the 188 showing parenchymal lesions, 29 were regarded as active on enrollment, and an additional 36 developed activity during their course of study. At Yale University, during seven years, parenchymal lesions were almost five times as numerous among the older entering students of the graduate schools as among the younger undergraduate freshmen. Race entered into the discrepancy as well as age.

The last American Student Health Association report gave interesting figures on the relative value of the old method of history and physical examination as compared with the newer method which adds the tuberculin test and the roentgenogram. In the year 1936–37 there were 24 colleges and universities with a total enrollment of 70,812 in which there were neither tuberculin testing nor X-ray studies. From these 24 institutions there were reported 20 cases of active pulmonary tuberculosis and 60 cases of clinically arrested disease. On the other hand, there were 13 institutions with an enrollment of 20,758, employing X-ray. They reported 40 cases of active disease and 106 cases of clinically arrested disease. The latter institutions in which tuberculin and X-ray were employed, although having an enrollment less than one third as large, reported twice as many cases of active disease and more than one and one-half times as many cases of clinically arrested disease. These figures support the accepted opinion that routine history and physical examination alone will fail to reveal many cases with lesions active or potentially so.

Along with studies of the incidence of infection in elementary school, high school and university students, there have been numerous studies in various other groups: in industry, CCC Camps, groups on relief, etc. While poor living conditions determine a higher incidence of tuberculous infection, the figures indicate that even in the less favored groups tuberculous infection is far from universal in young adult life. One cannot give a general figure for all, but the qualifying factors are known. They include age, sex, race, economic condition, locality, occupation, and known exposure to tuberculosis.

It is only relatively recently that the facts of lowered incidence of infection have been sufficiently appreciated as to affect the concept of the pathology of tuberculosis in adults. Heimbeck and

Scheel in Oslo, Myers and Opie in this country, were among the first to direct attention to a new state of affairs. Allen Krause was suggesting it twelve years ago. A new generation has been and is entering higher schools, colleges, universities, medical and nursing schools, and growing up outside these institutions, roughly one half of whom have never been infected with the tubercle bacillus and, therefore, may be expected to react to the first tuberculous infection with so-called primary infection types of disease, or what has been termed up to now, in this country, childhood type of infection.

As yet there have been but few satisfactory studies in the literature as to primary infection in adult life. Myers and his coworkers (6) in 1937 described and drew conclusions from 85 cases regarded as such. We quote some of the conclusions:

A positive reaction to tuberculin in a person who has previously shown no reaction to the test is the first obtainable evidence of the presence of tubercle bacilli in the body.

A few weeks are usually required after tubercle formation begins before the tissues are sufficiently sensitized to tuberculo-protein to react positively to tuberculin.

At the time the reaction of the tuberculin test becomes positive there usually is no external manifestation of tuberculosis. Symptoms are absent, there are no abnormal physical signs and roentgenograms rarely bring to light the location of the disease.

In a small percentage of those who in adult life become contaminated for the first time the focus of the disease when located in the pulmonary parenchyma attains a sufficient size to cast a shadow on the X-ray film which can be visualized with the naked eye. Such shadows usually become visible during the first three or four months after the infection has occurred. When they reach their maximum size they may show the same general appearance over a period of many months, after which they gradually recede. In some cases the shadows remain, leaving evidence of fibrous and calcium deposits, while in others they completely disappear.

The first infection type of tuberculosis as observed in our group of adults has resulted in no significant symptoms or abnormal physical signs throughout the entire course of development. Indeed the lesions in the majority of our cases would not have been known to exist had it not been for periodic tuberculin testing and the making of roentgenograms of the positive reactors.

Myers says further;

In our experience, adults in whom the first infection type of tuberculosis develops, even with considerable involvement in the pulmonary parenchyma and regional lymph nodes, do not require treatment in any form.

Apparently it makes little or no difference at what time of life the first infection with tubercle bacilli occurs, with reference to the evolution of tuberculosis in the

human body. When the first infection type of disease occurs in the second and third decades of life it is just as benign as when it occurs in childhood.

By roentgen examination alone it is impossible to differentiate between the first infection and the reinfection type of tuberculosis during the early period of development. Neither produces symptoms or abnormal physical signs. Therefore, a long period of observation is entailed. If the lesion proves to be of the first infection type, symptoms and physical signs do not appear and the shadow gradually recedes. If it is of the reinfection type, symptoms may appear later. Abnormal physical signs may be elicited. The shadow on the roentgenogram may increase in size or show evidence of cavity formation or both.

The concluding paragraph stated the following which bears upon a later portion of this paper.

In this student body of approximately 12,000 the number of students enrolled in the schools of nursing and medicine is a relatively small group, yet there is an overwhelming preponderance of lesions in this minor group, indicating to us that the problem of tuberculosis among young adults is most acute among those students who while in line of duty come in contact with tuberculous patients.

The subject of primary tuberculous infection in adults was one of three discussed at the last meeting of the International Congress on Tuberculosis held at Lisbon last September. The chief report was made by Scheel (7) of Oslo. It covered 229 cases, mostly women, from various services of the Ulleval Hospital. In 202 of the 229, erythema nodosum developed.

Scheel states that erythema nodosum is the early symptom par excellence of tuberculous infection. In preface he accepts that accord with this view is lacking in most countries but that in the Scandinavian countries and in France a great majority of cases of erythema nodosum are believed to have this etiology. Heimbeck found it in 39 of his 96 cases among nurses contracting tuberculous disease after being negative to tuberculin on entering training. This symptom is said to occur chiefly in women.

As to pulmonary lesions by X-ray, Scheel found them 67 times in the right lung field, 38 times in the left. In 77 instances they were small enough to be limited by a single rib or an intercostal space. The middle portion of the right lung in the vertical dimension was the seat of the greatest number of lesions, 29; the lower right lung field and middle left lung field were next with 13 in each. Hilum gland reactions varied considerably and were less often gross in adults than in children.

Another interesting very early symptom was an enanthem of the respiratory mucous membrane with symptoms of grippe.

"It is obvious," says Scheel, "that the great majority of primary infections run a benign course and cure themselves. Only thus can one explain the large number of individuals with positive tuberculin reaction in adult life who never develop clinical tuberculosis and who are unable to recall any period of illness which might be interpreted as due to tuberculosis." However, Scheel recognizes the possibility of dissemination of primary infection by direct propagation such as to the pleura, and by metastases by the blood, lymph streams and bronchi. Almost all of his cases were treated in hospitals and after their departure continued to treat themselves over a longer or shorter period. Nineteen developed pleurisy, 18 during the first year of observation and 1 during the third year; 2 patients died of tuberculous meningitis, 1 during the first year of observation and 1 during the second; 5 died of pulmonary tuberculosis, 2 during the first year, 2 during the second year and 1 during the fifth. The maximum of morbidity and mortality was during the first three years, particularly during the first year after infection. He recommends treating and observing the newly infected cases very closely since one cannot know their future resistance to the infection.

Badger and Spink (8) in their study of nurses described seven cases which they regarded as having primary infection types of disease. Amberson and Riggins (9) found six presumably of this type in their study of nurses.

From what has gone before it is seen that, as would be expected with only one half or fewer of young adults infected with the tubercle bacillus, evidence of primary infection is being found among them. Differentiation between the primary form and the superinfection forms of disease is difficult. The primary form can be suspected when the individual has been so closely followed with the tuberculin test that only a short period has elapsed after the change to a positive reaction, and the roentgenogram shows a lesion in the lungs previously not present, and found on observation not due to some nontuberculous infection.

Tuberculosis Among Medical Students

The title of this paper was chosen on account of the interest of this assemblage in pulmonary tuberculosis not only in young adults generally but among medical students and nurses particularly. The old passive attitude toward the disease among them is

outmoded. There has been an awakening of the public, and an increasing demand that hospitals and training schools assume responsibility for the protection of those given into their charge. Furthermore, the investment in each medical and nursing student is too great for disregard of any reasonable means to protect them against professional exposure and its results.

Numerous earlier reports usually indicated a greater incidence of tuberculosis among medical students than among the corresponding general population. In explanation, the emphasis was put upon the student's manner of living and upon his overwork, rather than upon his greater exposure to infection. With the newer methods of detection and with the improvement in the student's living conditions the emphasis is changing to degree of exposure.

Several of the leading medical schools have already inaugurated a program of prevention designed both to minimize exposure and to detect an acquired lesion in its earliest stage by the use of tuberculin and X-ray. Most such programs are of recent adoption, too recent to draw conclusions. There have been, however, a few experiences of more recent date and from them one can obtain a fairly good idea of the present situation.

Hetherington, McPhedran, Landis and Opie (10) at the 1931 meeting of the Association of American Physicians caused a stir with their report on "Tuberculosis in Medical Students" at the University of Pennsylvania. The entering students reacted to tuberculin to the extent of 85.6% and there was a steady increase to 98.2% in the fourth year. Of manifest pulmonary tuberculosis with symptoms there was one case in the first year, none in the second, four in the third, and nine in the fourth year. Of diagnoses of supraclavicular apical infiltration there was an increase from 3% in the first year to 10% in the fourth. Conspicuous pulmonary infiltration extending below the clavicle was not found in students of the first two years, but occurred in six students of the third year and in 13 of the fourth. In its final paragraph the report stated, "The number of young adults with apical lesions of tuberculosis increases gradually with increasing age, but the incidence of these lesions in medical students, increasing rapidly in successive years of the medical course, with astonishingly high incidences in students of the fourth year, indicates that they are peculiarly subject to grave tuberculous infection."

Curiously, at the same meeting Fitz (11) stated that 484 stu-

dents of the Harvard Medical School had been roentgenographed as part of a general physical examination and only one case of tuberculosis was detected.

In 1935 Hetherington, McPhedran, Landis and Opie (12) reported on a continuation of their work with the medical students of the University of Pennsylvania, the new examinations having been undertaken in 1931, 1932 and 1933, during which time approximately 400 medical students passed through the medical school. The incidence of tuberculosis was still notably high.

Since 1935 most serious efforts have been made to reduce infection among the medical students of the University of Pennsylvania, and tuberculin and X-ray have been used freely for diagnosis. A report sent last March by Dr. H. B. Lees (13), in charge of the Student Health Service, would indicate that results are being obtained. Whereas in 1935–36 there were 30 cases diagnosed tuberculosis by X-ray or otherwise, or 5.8% of a total of 514 students, there were, in 1936–37, 19 or 3.9% of a total of 481 students, and in 1937–38, 14 or 3.7% of 379 students of the three upper classes. Of the 14 cases in the school this year 12 are in the fourth year class. Dr. Lees hopes to start next year with almost a clean slate. In regard to tuberculin testing he states that during the last three years the medical students have shown about 70% of positive reactions to tuberculin the first year and 97 or 98% upon graduation.

In 1932 Herman, Baetjer and Doull (14) reported on tuberculosis among Johns Hopkins medical students. During the winter of 1929–30 all classes were tested with 1/10 mgm. of Old Tuberculin. Assuming as evidence of tuberculous infection either a positive tuberculin reaction (0.1 mgm. O.T.) or a lesion disclosed by X-ray, the authors found that the proportion of infection in medical students at Johns Hopkins according to classes was: first year 79%; seecond year 91%; third year 100%; fourth year over 98%. They combined figures from the Western Reserve School of Medicine with those of the Johns Hopkins and showed an average annual morbidity rate of 6.5 per 1000. It was concluded then that the evidence was insufficient to prove that medical students suffered a higher incidence of pulmonary tuberculosis than persons of similar age and economic status engaged in other occupations, but that such data as were available suggested that the student of medicine might be subjected to a higher risk.

On February 28, 1938 Dr. Herman (15) wrote that since 1926,

1132 students, including the class entering in the fall of 1937, have entered the Johns Hopkins School of Medicine. Of this number 16 have had outspoken pulmonary or pleural tuberculosis and one had tuberculosis of the urinary tract with no pulmonary lesion. In two the diagnosis of tuberculosis was very doubtful. Of the 16 students who developed tuberculosis, 2 had known tuberculous lesions prior to their admission to the school. The last case of active tuberculosis developing in a medical student at Hopkins was in March 1935.

Dr. Herman wrote further that at the present time a routine X-ray film is taken of the lungs of all medical students on admission. They are urged to have yearly check-up films and about 60% comply with the request. Routine tuberculin tests have not been made for several years but it is desired to reinstitute them.

Tuberculosis has not been a particularly major problem at the Yale School of Medicine. Among 427 students entering during eight years from 1930 through September 1937, six cases were diagnosed by X-ray as having parenchmyal lung lesions on admission. During the last five years the students have also been roentgenographed in the Spring of their final year, 219 in all. Three showed minimal apical lesions and one subapical disease. In addition, two of the 427 broke down during their course. Of the twelve students diagnosed, one was not permitted to continue beyond admission, two left the school for reasons other than health, two were treated successfully during one year and have continued their work without trouble, five underwent no special treatment and have continued well, one is now under treatment and one is too recent for a statement. Six of the twelve might be regarded as having possibly contracted infection or superinfection during the medical course, although one of them had previously been exposed at home, another had a frank primary complex on admission, and a third developed his pleurisy with effusion in his second year.

During the winter, letters have been received from several medical schools.

Dr. Sarah Morris has in operation a very comprehensive plan for the detection of tuberculosis at the Women's Medical College of Pennsylvania. Among other procedures all entrants are tested with tuberculin and, when not reacting, every six months there-

after until positive. X-ray studies are made of all students each year and more often if desirable. They are also made of those changing from tuberculin negative to tuberculin positive during the year. Tuberculin testing in successive years has shown that 100% react positively in the fourth year. On the other hand, the positive reactions on entrance from 1932 through 1937–38 fell from a maximum of 63% in 1933–34 to a minimum of 32% in 1937–38. As to lung findings, the 1937 survey showed in the school's enrollment of 107 students, 1 healed parenchymal lesion in the first year against 8 in the third and fourth years respectively. Of unstabilized lesions there was none in the first year but there were 4 in the fourth year. Of frank cases there was none in the first year against 1 in the third year and 2 in the fourth year. The last 3 cases were sent away for treatment.

At Columbia University (P. and S.), in addition to the complete history and physical examination, a single X-ray is taken of the lungs of all entering students. Late in the fourth year single films are again taken. Routine tuberculin tests have not been made but their desirability is being discussed. Dr. Flood (17) wrote that the medical students' record at the P. and S. for fifteen years terminating two years ago showed the incidence of recognized pulmonary tuberculosis to be 0.4%. A number of students known to have had clinical pulmonary tuberculosis before admission were not included. He remarks that the incidence of recognized active tuberculosis at the P. and S. is very considerably lower than that reported by some of the other medical schools.

From Harvard, Dr. Heath[18] wrote in February 1938,

> We do a tuberculin test on each entering student and, if the test is negative, repeat it annually. An X-ray of the chest is also made of each entering student. If the tuberculin test is positive we repeat the X-ray annually. This system has been in force only one year. Previously, tuberculin tests and X-rays were done on the entire first and fourth year classes. About 60% of first year students have positive tuberculins and about 85% of fourth year students.
>
> I cannot say exactly what our incidence of pulmonary tuberculosis is. Last year we sent three students away to sanatoria, this year none (out of a student body of 500). In addition we have four students who have definite X-ray evidence of pulmonary lesions but without clinical signs who are under strict supervision. I should say that annually four cases of active or inactive pulmonary tuberculosis are picked up. There is no doubt that tuberculosis is the most important organic medical problem in the medical school.

A letter was received last March from Dr. Barnett (19) of the Stanford University School of Medicine. The school in San Fran-

cisco has the students for the last two years, they being at Palo Alto up to then.

There were 420 students in San Francisco from the Fall of 1933 when records were first kept. Four developed active pulmonary tuberculosis, a little less than 1%. Six additional students showed X-ray evidence suggestive of active infection. Only one of these was put to bed. All recovered and have shown no further evidence of tuberculosis.

All students are examined physically and tested with tuberculin during the first year at Palo Alto. X-ray films are taken of all positive reactors and usually of most of the non-reactors. At the beginning of the third year and again at the end of the fourth year routine chest films are taken, and examination of the chest is repeated at the end of the fourth year. Tuberculin testing has not been repeated up to now after the first year, but this year routine annual tests are being started on all students negative to tuberculin the first year.

Dr. Stiehm (20) wrote last March of a rather remarkable experience at the University of Wisconsin.

Since 1933 there has occurred only one case of active tuberculosis among the medical students. The experience bears upon approximately 250 medical students who finished their medical training at Wisconsin and upon another 250 students who took only the first two years there. The students going through to graduation spend one week on the tuberculosis ward of the Wisconsin General Hospital, one week at a state sanatorium and one week at the Milwaukee County Sanatorium. During their tuberculosis experience they follow a strict isolation technique and wear masks and gowns when caring for the patients. All of their tuberculosis work is done during the senior year and except for contact with general ward patients in the junior year, they have very little contact with the disease outside the fourth year.

In addition to the physical examination a tuberculin test is given on admission. Those having positive reactions have a single roentgenogram of the chest and are re-examined during their student career at three to eight month intervals by fluoroscopy. Stiehm thinks that the medical students have very little opportunity for infection with tuberculosis and that this fact probably explains the small incidence of the disease among them.

At the New York University College of Medicine, all entering

students are tuberculin tested, and those students reacting are retested at intervals until positive. Routine roentgenograms of the chest are made annually regardless of the tuberculin testing. Dr. Connor (21), who is in charge of the Health Service, reports that the incidence of tuberculosis in students has not thus far proved to be excessive.

In 1935 Scheel (22) of Oslo published the results of his study of medical students from 1926 to 1934. All of the 1176 students underwent a period in the tuberculosis ward of the Ulleval Hospital and were tested by the Von Pirquet method, "often controlled by Mantoux." They were divided into groups, of which groups one and two are the most interesting. Group one comprised 361 students tuberculin positive before the exposure in the tuberculosis ward; group two, 207 students tuberculin negative before or during exposure.

In relation to exposure, the percentage of tuberculin positives during the previous year as well as during the first two months of exposure was 58%. Three to twelve months after being in the tuberculosis ward the positives numbered 81%. Like Heimbeck, Scheel finds there is a period of pre-allergy during the first six weeks of exposure and that the positive tuberculin tests due to exposure do not appear until after a lapse of about two months from the beginning. He finds that infection does not take place so rapidly in the medical students as among nurses, nor are the medical students infected with as much certainty.

By a statistical computation taking into consideration the period of exposure in the tuberculosis wards, Group 1, with a positive Pirquet before exposure, showed an annual average morbidity of 1.47%; Group 2, with Pirquet negative at the beginning of exposure, showed an annual morbidity average of 4.31%, almost three times as high.

Scheel goes on to say, "It has been thought that primary infection of adults produces grave clinical forms. Our experience is similar to that of Heimbeck, that the lighter forms are in the majority."

He reasons as to the importance of superinfection in an individual previously infected and therefore reacting positively to tuberculin: If superinfection often provokes new localizations of tuberculosis there should be an increase of morbidity when the tuberculin positive individuals continue exposed to new infection.

He quotes Heimbeck's experience wherein one finds the following numbers of tuberculous affections among originally Pirquet negative nurses during the six years after exposure: 59, 20, 8, 1, 1, 4; the manifestations are found during the first two years and particularly in the first year. In the nurses with positive Pirquet reactions the corresponding figures are: 7, 8, 3, 2, 3, 1. Scheel had the same experience with his medical students. While the morbidity was 6.5% in the first year and 3.9% in the second among the originally Pirquet negatives, the figures vary, but without increase, during the first years among the Pirquet positives.

To summarize the present situation as to medical students: they are, as a rule, less rapidly and less certainly infected than pupil nurses, but they still acquire infection to an excessive degree. The morbidity among them appears to vary. It seems alarmingly high in a few instances, but not in the majority of schools whose figures are known. Many of the leading schools have already instituted programs of prevention and case finding. Where a definite program is lacking there is an increasing consciousness of the problem and effort to cope with it. The mortality seems not unduly high, probably because the cases developing are apt to be diagnosed and treated early.

It is interesting that figures compiled by Miss Whitney (23) in 1930 from ten representative states as to the mortality rate from respiratory system tuberculosis among all occupations of gainfully employed males, showed the rate for physicians and surgeons to be among the very lowest.

Tuberculosis Among Nurses

Of recent years, tuberculosis among nurses has become a subject of considerable controversy. Danger of infection has been much emphasized: on the one hand that of primary infection, on the other that of superinfection.

Opinions are at variance: a few oppose admitting to the general hospital a pupil nurse negative to tuberculin lest she contract a primary infection and, through the acquired allergy, become a subject for superinfection disease; a few others oppose admitting a tuberculin positive pupil lest, already allergic, she acquire superinfection disease. Both attitudes are based upon a profound fear of superinfection. The majority feel that neither attitude is either practical or grounded upon sufficient evidence. Many,

indeed, believe definitely that an existing stabilized infection confers a degree of protection.

At the outset it should be stated that the problem presents itself chiefly in the relatively young student nurse in the general hospital, who has an experience in tuberculosis as part of her training, or who, without such planned experience, may be exposed to unsuspected tuberculosis in general wards.

It is still the consensus that the older staff nurse in tuberculosis institutions does not develop disease materially more than the general average of women of the same age. The most recent and careful study of this latter group was of 518 staff nurses at the Fitzsimmons Hospital, by Pollock and Forsee. (24) All were tuberculin positive. Only 8, or 1.5%, developed tuberculosis. These older nurses were apparently well protected againts new exogenous infection.

Numerous articles have been published in the past, most of them going to show the incidence of pulmonary tuberculosis among nurses to be higher than among comparable groups of women generally. The best of the more recent literature was summarized by Miss Whitney (25) in 1935. Differing circumstances bearing upon the various studies make it impossible to draw a clear conclusion as to the relative incidence of disease. It seems unreasonable, indeed, to expect a uniformity of figures in view of the differences in age, locality, living conditions, exposure, methods of calculations, etc. Some of the more recent articles, however, do give some clue.

Shipman and Davis (26) studied the nursing personnel at the University of California Hospital during the decade up to 1933. They definitely state that there was very little exposure to tuberculosis. Six per cent of 387 nurses developed active tuberculosis sometime during their training. Questionnaires were sent to 374 nurses graduating during the same decade. An additional 4% had developed tuberculosis after graduation.

All of the tuberculin testing was with 1/100 of a milligram, without the use of higher strength, The percentage originally positive was 60. Retesting after a lapse of a year or more showed 66% of positives. Of those who broke down, two were of the originally tuberculin negative. The others breaking down were from the originally tuberculin positive.

The relatively small increase in the number becoming positive

may be explained on the basis of relatively little exposure. On the same basis one might infer that the excessive breakdowns among the originally positive reactors might have been due to environmental factors and not so much to exogenous infection during training. The use of 0.01 mgm. of tuberculin as the maximum dose must have resulted in failure to detect a fair number of positive reactors.

Ross (27), in 1930, reported a study of tuberculosis among nurses admitted to the Manitoba Sanatorium in that province. Among 800 nurses in training in the province 6% broke down during their four year instruction, or 1.5% per annum. The number of cases occurring among nurses was in excess of that among other women. Ross also states that a great majority of the nurses broke down in training or just afterward; that the incidence of tuberculosis is not unduly high among nurses after graduation; that it is highest in hospitals; that it appears to be particularly high among very young nurses.

Carmalt Jones (28) in 1933 reported an incidence of 3% per annum during two years among a staff of 120 probationers, 25 staff nurses and 24 sisters in a New Zealand Hospital. All of the nurses did a three months' tour of duty at a tuberculosis sanatorium; all became Pirquet positive.

He compares the nurses' experience with that of 1125 women of much the same age in three other schools not concerned with nursing. Among the latter there were only 2 cases of tuberculosis, one of them fatal. There were records of two deaths in ex-students from one school four years after graduation.

Mariette (29) in 1936 reported on an intensive study over a long period at the Glen Lake Sanatorium, Minnesota. He is a strong partisan of the idea of the protective influence of an existing infection. He accepts that there is a certain tuberculosis hazard in the nursing profession and urges all reasonable measures to meet it. He now roentgenographs the nurses at three month intervals to detect the earliest manifestations of disease.

In 1934 Geer (30) of St. Paul published the experience at the Ancker Hospital. From 1920 to 1928, 4.5% of the nurses developed tuberculosis, three times the normal expected incidence. After 1928, all incoming nurses were tested with Tuberculin and retested every six months. Roentgenograms were made on admission and subsequently with a change to a positive reaction. From Septem-

ber 1928 to September 1930, 5.5% of the nurses developed tuberculous disease. An extremely rigid technique was introduced in the Spring of 1931. Presumably as a result, only 1.6% of nurses developed the disease from September 1930 to the writing of the report in 1934 as against 5.5% during the two years prior to the rigid technique.

In 1936 Amberson and Riggins (9) published a five year study in tuberculosis among students in the Bellevue Hospital School of Nursing, New York City. The average age on admission was 18 to 20 years. Of 539 candidates 57.9% were positive on admission either to 0.1 mgm. of Old Tuberculin or to 1 mgm. when negative to the smaller dose. About one third of those failing to react to 0.1 mgm. did react to 1 mgm.

The originally tuberculin negative were retested every six months until reaction was noted. Of a group of 143 followed six months to three years, 37 became tuberculin positive during he first year of training, 37 during the second, and 10 during the third. Among 70 negatives followed for the full three years of the course all but 10 became positive. Thus it would seem that the majority of presumably uninfected nurses become infected sometime during their course which includes one month on a very busy tuberculosis service at the beginning of the second year of training. Here the nurses wear gowns when ministering to patients but face masks are not worn. Cleanliness and especially frequent washing of the hands are urged upon all nurses, but "contagion technique" is not employed.

During the five year study 8 cases of tuberculosis came to light: 6 with pulmonary lesions; 1 with serofibrinous pleurisy and 1 with spondylitis. One case was diagnosed during the first year of training, 3 in the second and 4 in the third.

In September 1937 Badger and Spink (8) reported a five year study of student nurses in the Boston City Hospital, begun in January 1932. Thereafter, all nurses entering training underwent complete physical examination, quantitative tuberculin tests and stereoscopic X-ray examinations of the lungs. Only those failing to react to 1 mgm. of O.T. were declared negative and yearly tests were repeated of non-reactors. Stereoscopic X-ray examinations were repeated yearly on all student nurses, and oftener when indicated.

Of 470 nurses, 57.11% were positive to tuberculin on admission.

Of 126 nurses who finished their three year training and who were 66% positive on admission, 90% were positive on discharge.

There were 273 nurses, of whom 126 completed their course of training and 147 remained in training one year or more. Among the 273, 59.3% were positive to tuberculin on admission. Eight tuberculous lesions were observed in this entire group. One case developed among the 162 initially positive reactors; 7 cases developed among the 111 initially tuberculin negative.

From this limited experience the authors agree with Myers that the first infection type of tuberculosis is usually a benign form. However, a few small primary infections progress. Whether the lesion is benign or destructive cannot be determined at first, and all must be judged and followed with extreme care.

Stiehm wrote to us on March 1, 1938, that during the last five years there has not been a single case of active tuberculosis among 76 pupil nurses at the Wisconsin General Hospital at Madison. The same strict isolation technique is employed with them as with the medical students. They are required to work only 8 hours per day and only 4 to 6 hours are spent on the wards. The nurses are closely followed by tuberculin and X-ray. The percentage of infection is increased by about 10% during the three year period of training. The known exposure is during a two week period of training in the tuberculosis ward of the hospital.

The Yale School of Nursing has not suffered particularly from tuberculosis in recent years. Of 385 students roentgenographed on admission from September 1930 through September 1937, six were diagnosed as showing parenchymal lung lesions. Of the six, three were sent away for treatment immediately or within a few months, three continued their work and remained well. Of 191 students again roentgenographed on graduation during the last five years, one showed a new minimal lesion for which she successfully underwent treatment, a second showed an apical lesion which has remained arrested during four years. One student developed pleurisy with effusion during her course and returned to work after one year of treatment. It should be stated that these pupils average about 23 years of age. They have experience in a tuberculosis ward and during three weeks in a tuberculosis hospital.

To Heimbeck (31) of Oslo there is owed a debt for much of the present interest in tuberculosis among student nurses. His painstaking studies were begun in 1924 with modern methods. He has

published a number of articles, the last that we have found being in summary form in December, 1936. The studies have been upon nurses entering and going through the Ulleval Hospital in Oslo where there is a large tuberculosis ward in which all pass a portion of their training period.

In starting his observations Heimbeck divided the nurses into two groups: Group 1 comprised those who on entering training were "allergic, Pirquet positive, infected, without any symptoms of tuberculosis either in their earlier days or subsequently on investigation, who had passed through the stage of their primary infection without becoming ill." Group 2 comprised those who were "not infected at the time of entering training, Pirquet negative."

The groups were followed year after year. Some started in 1924, some in 1925 and so on, the latest in 1935. Every nurse was exposed to tuberculous infection and everyone became infected within the first three years in the hospital.

An interesting finding was the difference in morbidity between those Pirquet positive on entering training and those Pirquet negative: 625 of the former with 2659 observation years showed 27 instances of disease and no deaths; 280 of the latter with 561 observation years showed 96 instances of disease and 10 deaths.

Among the 27 instances of disease in the originally Pirquet positive group there were 8 of pleurisy, 4 of pulmonary tuberculosis with positive sputum, 7 with pulmonary inflammation with negative sputum, 7 of erythema nodosum. Among 96 instances of disease among the originally tuberculin negative there were 24 cases of pulmonary inflammation with negative sputum, 13 of pulmonary tuberculosis with positive sputum, 16 of pleurisy, 39 of erythema nodosum, 3 of meningitis and 2 of tuberculosis of the bronchial glands.

In 1934 Myers, Diehl and Lees (32) presented a particularly strong appeal for the protection of nurses from infection by every possible means. They showed graphically how in a school of nursing where there was a tuberculosis service and no protection of any avail for the nursing students, the positive reactors increased from 30 to 35 per cent on entrance to over 95% on graduation. In contrast, students entering the School of Education in the University of Minnesota where there was no exposure to tuberculosis showed only a 4% increase between the first and graduating years.

To summarize as to nurses: Although thoroughly satisfactory figures are not available to indicate the incidence of tuberculous disease among student nurses as against the similar age group of the general population of women, the prevailing opinion is strongly that such incidence is higher in the student nurse. Certainly this is the situation locally at times when it actually becomes necessary to appoint special committees to investigate conditions.

Tuberculin studies almost without exception indicate an accretion of infection year by year quite out of proportion to the general population. This is found to be most marked where student nurses are in contact with known cases of tuberculosis as a part of their training. To a lesser degree it is found in hospitals where tuberculosis is not knowingly admitted.

The hazard is essentially to the young pupil nurse in the general hospital rather than to the older graduate.

To quote from Carmalt Jones: (28) "There appears to be an unduly high incidence of tuberculosis among young nurses. They come from sheltered families, at a period of life when according to clinical experience the incidence of pulmonary tuberculosis is high among women; . . . they are called upon to work unusually, though not unduly hard, and they are apt to tax their strength by indulgence in amusement which shortens their rest. In these circumstances they are brought into intimate contact with declared cases of tuberculosis and also with open and undeclared cases. It is the clear duty of hospital authorities to protect these women."

Discussion

It seems clear that the earlier concept of universal infection with the tubercle bacillus by the age of 15 years no longer holds. There is today a generation of young adults of whom roughly a half or more are not allergic to tuberculin. A literally vast number of tuberculin tests supports the truth of this statement. On the other hand, one cannot prove that all individuals negative to tuberculin have escaped earlier infection, since there is evidence that skin hypersensitiveness may wane or disappear.

As to the tuberculin test: In this country most of the testing of young adults has been by the intracutaneous method of Mantoux. The earlier tests were performed with Old Tuberculin. More recently the Purified Protein Derivative (P.P.D.) of Long and Sei-

bert has been widely used. The differences in the results with the two are not sufficient to affect the conclusions drawn. In many instances the Mantoux recommendation of three tests; 1/100 mgm., 1/10 mgm. and finally 1 mgm. has not been strictly followed. A two test method is often employed, the first with 1/100 mgm. of O.T. or 1/10 mgm., and the second or final test with 1 mgm. of O.T. With P.P.D., as generally recommended, the final dose is equivalent to 1 mgm. of O.T. and the weaker of first dose is equivalent to 1/250 of that strength. A considerable number of individuals require the full dose to bring out the reaction. Badger found that 19% of 184 ultimately positive cases failed to react to 1/10 mgm. but did react to 1 mgm. Amberson found that about one third of those who failed to react to 1/10 mgm. did react to 1 mgm. At Yale there has been a large experience with about 4500 students of whom approximately 30% of those finally positive did not react to the smaller dose of P.P.D. but did react to the larger dose. It is generally accepted that 1 mgm. of O.T. or its equivalent must be used intracutaneously to evoke the maximum number of positive tests. The Von Pirquet test is not equivalent to 1 mgm. of O.T. intracutaneously. Figures as to the absence of allergy on the basis of tests with less than 1 mgm. of potent tuberculin or its equivalent intracutaneously must be regarded as too low.

Is a negative tuberculin test a reliable index of absence of tuberculous infection? Generally speaking, it is so regarded, although a few conditions, among them measles, influenza, miliary tuberculosis and terminal stages of pulmonary tuberculosis may at times be accompanied by a temporary anergy. The reason is not clearly understood. These states would but rarely confuse the result in ordinary case finding. Furthermore, and we believe that this fact has received too little attention, there is a not inconsiderable number of persons who, despite frank calcium in the lungs or tracheobronchial glands, fail to react to the full strength of tuberculin. In these instances the infection is assumed to be healed, or completely walled in. Whether such persons should be regarded as devoid of the protective effect of the earlier infection is still a question.

Is intensity of reaction an index of severity of infection? The majority of observers believe that it is not. On the other hand, Hetherington, McPhedran, Opie and Landis (1) found that in

children the majority of those showing pulmonary lesions reacted to 1/100 of a mgm. of O.T. Howe (33) has shown that there may be a considerable daily fluctuation in skin sensitiveness to tuberculin.

Certain views have come to be generally accepted. One is that even the best history and physical examination will not reveal primary infection disease in adults any more than in children. Another view is that history and physical examination alone will miss very many cases of minimal superinfection disease. Boynton and her co-workers (34) among 126 cases of adult type pulmonary tuberculosis diagnosed by X-ray and clinical observation among University of Minnesota students from 1931–35, found abnormal physical signs present in only 10% of the fibrotic and minimal cases, and in only 23% of the moderately advanced. Fellows (35) in 280 early cases of pulmonary tuberculosis diagnosed by X-ray found abnormal physical signs in only 21%. A third accepted view is that primary tuberculosis and also many cases of superinfection disease will not be accompanied by symptoms of severity sufficient to take the individual to the physician until the disease is in an advanced stage.

Incidentally, the last view goes far to explain why our sanatoria the country over admit about 5 cases of advanced disease to one of minimal. Until the X-ray, with or without tuberculin is more generally employed by physicians this deplorable state will improve but little. It is our belief that for the promotion of early diagnosis of tuberculosis, maximum emphasis should be put upon the education of the oncoming generation of physicians as to the particular importance of the X-ray as the only means by which, as a rule, the small lesion will be detected.

The best present method to detect early pulmonary tuberculosis in the lungs of students appears to be that which employs both the tuberculin test and the roentgenogram in the beginning, and which then follows the positive reactors with roentgenograms, and the non-reactors with tuberculin until a change to positive takes place. Once the change has taken place the positive reactors too should be followed with roentgenograms.

Many studies, although not all, indicate that more tuberculosis develops among those tuberculin negative on exposure than among those tuberculin positive, but the long-voiced fear lest primary infection in adult life play particular havoc seems not to be borne

out. Primary infection in adults, other things being equal, appears to be distinctly less grave than in infants and no more grave than in older children. The great majority infected in young adulthood show no symptoms and no notable ill effects. However, the number in whom the effects are serious is apparently far from negligible. To what extent these later primary infections influence the high morbidity and mortality rate among young adults has not been definitely determined. Much is still to be learned in this regard.

The question enters as to whether an earlier infection manifested by definite allergy gives any protection from further exogenous infection. Where the number of observations is sufficiently large and sufficiently controlled there seems to be little argument. The Norwegians are convinced of this protective action, and Heimbeck and Scheel are so certain of it that they vaccinate originally negative nurses and students with B.C.G. and are not satisfied unless allergy is produced therewith. Indeed, Heimbeck's (36) last sentence in an article in 1933 was, "Tuberculosis-allergy is tuberculosis immunity, regardless of whether it is produced by tubercle bacilli or B.C.G."

Allen Krause has always maintained that allergy is accompanied by relative protection, and we personally agree. If one discards this concept he disregards a great mass of painstaking experimental work and a long series of attempts at active immunization of man and cattle. No one maintains that the protection conferred by an existing infection against exogenous infection is absolute. But one is justified in maintaining that relatively much protection is conferred; enough, in the opinion of many, to more than offset the harmful effects of allergy. However, the point seems relatively unimportant unless one acts upon his conviction to the extent of excluding either the allergic or the non-allergic student. What really is vital is the avoidance of infection.

Infection of nurses and medical students is presumably most often by aspiration. Scheel (7) cites the experiments of Chausse and of B. Lange to the effect that larger droplets adhere to the tracheal and bronchial mucosa and are expelled by the ciliated cells; that smaller droplets containing only 1 bacillus or a few units may be inspired into the lung alveoli. Slight infections would accord with relatively long periods before allergy develops and lesions become manifest by X-ray. Is it not perhaps assum-

able that the positive tuberculin reactions acquired by students may be from very few bacilli in one institution and, therefore, accompanied by but little manifest lung pathology; that in another institution more bacilli are offered, and to the degree of producing an alarming amount of disease? In both instances there might be a parallel increase in the number of positive reactors to tuberculin.

What can or should be done to reduce the infection in medical students and nurses to a minimum? Geer (30) instituted what is termed a strict medical aseptic technique to apply alike to all who come into contact with tuberculous patients: nurse, student, physician, personnel, visitor. Not only the usual gown is worn, but masks and caps. Details cannot be given here, but suffice it to say the technique goes far beyond any attempted previously. Stiehm at Wisconsin also carries out a rigid technique and Myers urges the utmost in precautions.

Institutions will go to differing lengths to prevent infection, but certain minimum measures should always be taken. There should be a contagion technique, at least to the point of wearing of special gowns and frequent washing of hands; methods of autopsy rooms and laboratories should be carefully scrutinized; every medical and nursing student, before beginning work with tuberculous patients, should be carefully instructed as to the hazards and as to the importance of technique, especially that of the patient's completely covering his mouth with sufficient layers of paper to retain expelled droplets (Jennings 37); living and working conditions should be thoroughly healthful. In addition, every effort should be made to discover tuberculosis in unsuspected cases admitted to the general hospital for conditions other than tuberculosis. The ideal plan to this end would be a roentgenogram of all cases on admission regardless of diagnosis, and routine examinations of sputum, whenever present, for tubercle bacilli. The unrecognized case of open tuberculosis in the general ward is a serious menace. The findings of a routine chest survey by X-ray of all patients entering the University of Michigan Hospital during eleven days are interesting in this and other regards (Hodges 38).

Finally, there should be carried out a plan of tuberculin testing and roentgenographing every medical student and pupil nurse, in order that infection acquired will be detected at the earliest mo-

ment. There is no good medical school without at least one teacher vitally interested in pulmonary tuberculosis. The time and money required for tuberculin testing and roentgenographing the relatively small number of students and pupil nurses is not great. It is small compared to the cost of one case out of control.

The treatment of pulmonary tuberculosis discovered among these students requires discrimination, judgment and experience on the part of the physician. Manifestly active cases should be put under treatment at once. In other instances, symptoms are vague or lacking, yet the small pulmonary infiltrations are potentially dangerous and should also be treated promptly and strictly. Only when the lesion is judged to be stable and fibrotic is it justifiable to postpone treatment pending a period of observation. In every case, observation should be at frequent intervals, at first with a roentgenogram every two to three weeks and close clinical study until the stability of the lesion is determined. Apparently stable lesions should be followed with roentgenograms for many years, at first every three months, and never less than once a year. As a part of the clinical study, examination of the fasting stomach contents, obtained in the morning by lavage, is to be recommended when the patient with a pulmonary infiltration reports that there is no sputum.

Probably the time is not far distant when public opinion will force the most thorough measures on hospital authorities. Already in certain states tuberculosis among hospital personnel is being debated as to its compensability.

There is another value to a case finding program among students as great perhaps as that of prevention, namely the education of the student himself. As one personally and vitally concerned in the program of prevention, he absorbs two basic ideas that one wishes to inculcate: prevention and early diagnosis. Through the emphasis upon them as applied to him personally the student can scarcely fail to be impressed.

Conclusion

Tuberculous infection in young adults in this country and abroad is by no means universal. In this country at large, roughly speaking, 50% of the white population under the age of 20 do not react to tuberculin. In some sections, as the Middle-West, the percentage of positive reactors is notably lower. A far-flung and

increasingly effective effort is under way to detect early tuberculous infection and disease by the addition of the tuberculin test and the roentgenogram to the older methods.

The medical student and the pupil nurse are more exposed to tuberculous infection during their training than are those in other professions and occupations. This fact is attested by the disproportionate increase in positive reactions to tuberculin during their training. Infection in them may produce a primary type of lesion in the non-allergic individual or the superinfection type in the allergic. Studies strongly suggest that recognizable lesions occur more frequently in the non-allergic than in the allergic. Allergy may be said to be associated with a definite protective influence within certain limits.

The severity of infection of nurses and medical students appears to be decreasing owing to the greater application of methods to prevent exposure, improved diagnosis of the acquired disease in its earliest stage and elevated living standards. A greater and more widespread emphasis on prevention of infection and on early diagnosis, particularly by tuberculin and X-ray, should reduce the hazard of the student period to that of the general population, or even lower. With present knowledge the accomplishment of this reduction is not merely a possibility; it is a direct obligation upon institutions concerned.

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URINARY STONE. SOME PRESENT-DAY CONCEPTS*

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Though the occurrence of calculi in the urinary passages has been noted since the earliest medical records, and the disabilities caused thereby have called forth innumerable efforts toward relief by each succeeding generation of surgeons, it is only of very recent years that medical science has been able to bring forward any reliable data tending to explain; firstly, *why* calculi form; and secondly, *how* they form. During the past 10 or 15 years, however, new concepts have appeared, themselves leading to a number of exact observations which in turn have thrown real light on some of the many aspects of this intricate subject. Therefore a report of progress may be found opportune.

The suggestion that urinary calculi may be caused by the ingestion of improper substances or by taking too large an amount of substances otherwise harmless is of great antiquity as seen in the many writings on the relation of stone to various forms of diet or of waters. Such ideas far antedated knowledge of what we call metabolism today, and were based wholly on supposititious cause and effect. But, however lacking in scientific basis such ideas may have been, there remain today two incontrovertible facts out of the mass of conjecture. First, there are regions in the world in which calculous disease is so prevalent as to be truly endemic, and second, there are races such as certain blacks in South Africa in whom this disease practically never occurs. Throughout other portions of the globe stone formation varies in incidence, both in place and in time, and quite recently there is reported on good authority a striking wave of increase of lithiasis in Central Europe. Insurance statistics quote a mortality rate of from 3 or 4 to as high as 25 per million deaths in various countries or in parts of the same country.

Such facts as these make it immediately evident that the problem of calculous disease is composed of many elements, and that we must expect to deal with varying biological and chemical condi-

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tions and interactions in trying to solve its causes. But except for such general information as above nothing remains out of the past, of scientific value today.

At about the end of the first decade of the present century there appeared several new concepts in physiology and in physiological chemistry which have greatly influenced medical and scientific knowledge, giving us firm ground for the first time for the explanation of many phenomena which before had been obscure or lacking proper correlation. I need only mention here such epoch-making contributions as those of L. J. Henderson on "The Blood" and on "The Fitness of the Environment," and the charmingly convincing ideas of W. B. Cannon related in his book on "The Wisdom of the Body." Here are discussed in extenso the factors, physiological and chemical, which maintain the marvelous stability (homeostasis) of the various bodily systems, especially that of the blood—a stability continuously necessary for existence of the human body. To be added to these more general writings are those of such men as Cushny who has given us the present theories of "The Secretion of Urine" followed by the more specific contributions of van Slyke and Richards. To all this has been added the new knowledge of the Vitamins, especially at the hands of Mendel, Collip, Wolbach, and many others, as well as contributions on the surprising action of various of the endocrine glands, as found in the instance of the parathyroids, by the investigations of Aub, Bauer and Albright.

These newer concepts point out the extreme importance of physiological and chemical stability of all bodily systems, demonstrating clearly the methods of various sorts—chemical, nervous or other—by which this stability is maintained under the various stresses and demands made from time to time by the changing external and internal environmental needs.

As described by Cannon:

> The coordinated physiological processes which maintain most of the steady states in the organism are so complex and so peculiar to living beings—involving, as they may, the brain and nerves, the heart, lungs, kidneys and spleen, all working cooperatively—that I have suggested a special designation for these states—homeostasis. The word does not imply something set and immobile, a stagnation. It means a condition—a condition which may vary, but which is relatively constant.

He then discusses the fluid matrix of the body—the blood, lymph, and cellular fluids—the constancy of the water and salt content of the blood—the homeostasis of blood sugar, proteins, fat, and

calcium, and the remarkable delicacy of the bodily arrangements for maintaining the neutrality of the blood.

When applied to such a phenomenon as the occurrence of a stone in a kidney, such physiological knowledge as this furnishes the fundamental concepts with which any explanation of this occurrence must be in agreement. One may fairly argue as follows: A stone is not a foreign body—except possibly in the surgical sense—for it is made up of substances all of which are present in the blood stream in one form or another. We know, however, how absolutely important for health is the constancy of the blood stream both in a chemical as well as a physical sense, that is, its neutrality. We have learned also something of the influence of the kidney in helping to maintain this constant state of the blood by acting as an excretory organ. It follows that at one time or another and under very varying conditions of the general body, substances will be presented to the kidney for elimination now in large amount, now in small, and frequently associated with marked differences in the amount of fluid in which they are dissolved. And even though at times, given the presence of some condition acting as a *nidus* on which crystals may be deposited, such substances are found to have changed their physical state from being in solution to that of precipitation after reaching the spaces of the kidney itself, still at all events the homeostasis of the blood stream has been maintained.

For an explanation of the actual chemical conditions within the kidney leading to the formation of a calculus we must look to physical chemistry; and here, though there exists a certain amount of knowledge on the interactions of crystalloids and colloids, or on the influence on the solubility of one substance of the presence of another, exact observations applicable to any single instance await future discoveries. The one certain fact underlying all others is that some condition or substance must exist within the kidney, which will serve to initiate the crystalline deposits which eventually form the stone.

The substances of which calculi are composed are rather sharply divided into two groups: *The smaller*—1. derivatives of proteins as cystine xanthin and uric acid; *the larger*—2. substances containing calcium in some combination such as calcium and magnesium with phosphorus or in combination with oxalic acid, as calcium oxalate.

We have no exact knowledge concerning the causation of the first group—only theories, which cannot be profitably discussed here. There is more to be said for the calculi containing calcium in some form, as this is one of the elements of the body in regard to which we have some metabolic data. Besides the great importance of calcium in the growth and repair of bone, for the teeth, and for the function of the nervous system, we know it to be under the hormonal control of both the thyroid and parathyroid glands. Deposited in the bones, from which it is readily mobilized under a variety of influences, it is present in the blood in at least two forms, the ionized and the non-ionized—the calcium proteinate. Furthermore, pathology has long ago demonstrated the early and easy deposition of calcium in any area in which the tissues have become avascular, with fragmentation of the cells and intercellular substance. The administration of thyroxin has been shown to cause definite loss of calcium from the body, while the action of the parathyroids causes a reduction of the ratio of calcium to phosphorus in the blood. Furthermore, the continuous intake of a large amount of calcium, as under the régime of the Sippy diet, is frequently accompanied by renal stones which contain this substance.

As to the suggestions regarding the causation of stone, it has been thought in the past that the presence of obstruction within some part of the efferent urinary passages causing stasis might predispose to the precipitation of salts which otherwise would be held in solution. But very many cases of calculi, especially when small and early in their growth, are found in which there is no evidence of antecedent mechanical obstruction to pelvic or ureteral peristalsis. Stasis is probably more often the result of the stone than its cause.

Another suggestion relates to the ratio between crystalloids and colloids of the urine; the colloids by adsorption being assumed to hold the crystalloids in a supersaturated balance which is easily upset by an excess amount of the latter or a lessened amount of the former. It may well be that the crystalloids so held will be deposited on the surface of a stone once it has started to form, but this theory tells us nothing as to just what it is that sets the process in action.

In the third case there are those who hold that bacterial infection is the antecedent cause of stone, but this ignores the many in-

stances seen in the clinic in which no cultural evidence of organisms is to be had. We know that there are many instances of renal stone which are sterile. This is not to say, however, that infection bears no relation to stone, for we are very familiar with instances in which, the urine being alkaline due to some urea splitting bacterium, phosphatic stones recur with great speed and frequency. It is not clear, however, in such cases that the infection preceded the appearance of the first stone, for only too often both have been present long before the patient appears for examination.

A fourth condition as a result of which stones are found to form is related to endocrine dysfunction of the parathyroid glands. Here we are on firmer ground. Overaction of the parathyroids has been shown to cause a marked disturbance of the calcium-phosphorus ratio in the blood stream—a breakdown of the homeostasis —and to be accompanied by lesions in the bones in localized areas in which there is marked loss of calcium (osteitis fibrosa cystica). Along with this mobilization of calcium and consequent increase in its amount in the urine, there are changes in its phosphorus content as well. Clinical studies have shown the presence of calculi in well over 50% of instances of hyperparathyroidism. On investigating cases of urolithiasis serially, however, it is found that a diagnosis of parathyroid dysfunction can be made in only about 5% to 7% of the cases. We conclude, therefore, that though the disturbance in the calcium phosphorus ratio in the blood stream caused by hyperparathyroidism results frequently in the appearance of calculi in the kidney it is a cause which is rather rare in the total incidence of stone.

The last and most important state which, since the observations of Mendel and others, has been known to be accompanied by nephrolithiasis is that caused by a deficient bodily intake of vitamins, especially A, and to a less extent D.

Vitamin A deficiency causes an atrophy of epithelium and its replacement by keratinized cells. Its absence causes a starvation which is specific for many epitheliums. To quote Wolbach: "The consequence (of this starvation) is atrophy, which progresses to a state wherein the cells, although having the appearances of viability, become inert in physiologic activities and in their role of covering membranes. An invariable sequence in pathology is that a break in the continuity of a tissue is followed by reparative proliferation. In vitaman A deficiency the basal cells normally

concerned in maintaining the integrity of epithelium respond by active mitotic division. As the basal cells have a focal distribution in all nonstratified epitheliums, the next effect of the deficiency after atrophy is the appearance of scattered areas of proliferative activity beneath the original epithelium. The new (reparative) cells by their continued growth undermine and replace the original epithelium and, regardless of previous function and morphology of the region, develop into a stratified keratinizing epithelium."

Such cellular formation is directly comparable to keratotic areas of the skin of the old with which we are all familiar and which, in their superficial layers at least, take on the aspect of an inert foreign material.

Along with these epithelial changes which are most marked in the respiratory tract, the alimentary tract and the genito-urinary tract, there occurs in vitamin A deficiency a slowness in the regeneration of the visual purple of the retina. Thus is caused hemeralopia (night blindness)—and it is interesting that the test to dark adaptation has become one of the most delicate methods of determining a lack of this vitamin.

Twenty-four out of twenty-five patients having calculous disease were shown by Ezickson and Feldman to have a pathological ocular response to the dark. Giving these patients a more liberal amount of this vitamin, however, failed to improve the ocular condition. In animals, however, all workers have been able to show not only a return of the changed epithelia to a normal configuration on resuming a normal diet, but also, as so thoroughly demonstrated by the observations of Higgins, there is caused in many instances at least, a disappearance of the renal calculi. Following this lead Higgins has endeavored to relieve the condition of urolithiasis in human beings by the exhibition of a dietary high in vitamin A, with acid ash, accompanied by acidification of the urine to a pH as low as 4.5 or 5. Some diminution of the calculous formation has resulted, though this favorable effect is by no means constant or universal.

Turning now to local conditions in the kidney itself there has recently been brought forward some very important work by Randall which throws much light on the immediate pathogenesis of stone. From a large amount of autopsy material carefully examined he has been able to demonstrate lesions at the apex of the renal papilla consisting of a calcium plaque underneath the

epithelium on which, following erosion, stone-forming crystals will be or have been deposited. Without question such lesions represent the long assumed nidus which is the necessary starting point for the subsequent deposition of crystals eventually forming the calculus. Such conditions are shown also to take place without stasis of urine, and also on microscopic examination to be without evidence of inflammation.

Observations such as these are of the greatest importance for they lead us properly to undertake a much more thorough microscopic investigation of each renal papilla than has ever been the custom of the pathologist in the past. As Randall puts it, "the pathology of the renal papilla has yet to be written."

At first thought this actual demonstration of a focal lesion which acts definitely as the nidus for subsequent deposition of substances in crystalline form leads us to assume that this area is actually a localization of a vitamin A deficiency. But the histology does not bear out this assumption, for it does not show the keratinizing process characteristic of the vitamin A deficiency as we know it. On the contrary the description of Randall's material is as follows:

The Calcium Plaque: Approximately midway between the tip and the base of the papilla, underneath the epithelial covering, is an area, measuring 2.5 mm. in length and varying from 0.1–0.3 mm. in width, composed of dense connective tissue. The surface of the papilla over this area is somewhat irregular. The blood vessels in this location are less numerous, and those present are partially obliterated by the surrounding dense connective tissue. Some of the collecting tubules are devoid of lining epithelium, while other tubules show cells evidencing degenerative changes. In the portion of this region nearest the tip there are a number of small areas showing granular detritus. In this location are seen two small irregular deposits of purplish-staining material measuring approximately 0.3 by 0.03 mm. By special staining methods these deposits proved to be calcium. These calcium deposits, or plaques, are separated from the surface of the papilla by a thin irregular layer of connective tissue and covering epithelium. Where the calcium is less dense it occurs in rings, definitely deposited in the basement membrane and spreading into the ground substance of the surrounding connective tissue.

Through the papilla, but especially near the tip, there are areas showing an increase of interstitial connective tissue. Some of the blood vessels show narrowing and irregularity of their lumina. The cortex and medulla show no noteworthy lesions. The walls of the convoluted tubules show no calcium deposits. The larger vessels show a moderate degree of arteriosclerosis. There is no microscopic evidence of infection in this specimen.

Calculus on Plaque: Near the tip of the papilla, 0.3 mm. beneath the surface, there are irregular calcium deposits over an area 2.2 by 0.6 mm. Near these de-

posits, on the surface of the papilla, there is an irregular calcium plaque measuring approximately 0.4 by 0.1 mm. To the outer surface of this calcium plaque, and only to the plaque, is attached an irregularly shaped calculus measuring 1.75 by 0.8 mm. This stone, by special staining methods, was proven to be composed of calcium phosphate, while the plaque on which it grows stains for calcium but not for calcium phosphate.

This is not the occasion to indulge in speculation. It will be evident, however, that for the further study of the diverse problem of urolithiasis we have now a definite starting point. The question will now be: What conditions can be found which will cause a nutritional alteration of the cells in the renal papilla leading to subsequent deposition of substances brought to the urine by the blood? We are beginning to learn something about the vitamins, something about the action and interaction of the endocrine glands; we still need much further light on the normal and abnormal calcium metabolism, however. When it comes to the significance of a substance such as citric acid or the citrates in the bodily homeostasis or the action of such enzymes as phosphatase, we are still ignorant. But in the pathological changes of the renal papilla we can visualize much of great promise for future discoveries.

MODERN METHODS OF TREATMENT OF DISEASES OF THE NERVOUS SYSTEM*

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It is not many years since neurology was widely considered a purely diagnostic specialty—a *meditatio morbis*. One can look through the pages devoted to nervous diseases in almost any textbook of medicine written before the War, and scarcely find a single suggestion of treatment beyond arsenic, strychnine, bromides and electricity, aside from the more obvious indications for surgery.

Yet there are specific and effective forms of treatment for neurologic diseases, and their number has shown an astonishing growth during recent years. Since so few of them have found their way into the common body of medicine, I have thought it might interest this audience to hear a review of them. In assembling such a summary, I find that, as a matter of fact, there is so much ground to cover that certain important territories will have to be omitted entirely.

Three large and significant fields about which I shall say little are surgical. They are the territories of the treatment of injuries of the nervous system, of the surgery of tumors, and of operations on the sympathetic system. Any brief summary would fail to do them justice; moreover, the story of their successes has often been brought before the medical public, and recent authoritative books are available on each (1, 2, 3).

As a fourth subject, I shall leave psychiatry and psychotherapy entirely out of account, as being outside of may own sphere of competence. In passing, however, I should like to pay tribute to the rising standard of psychologic understanding and interest among practitioners and students of today. Though startling innovations have been rare, there is far less quarreling over doctrinal differences, and far more devotion to an unprejudiced appraisal of the patient's needs of various kinds, than was the case twenty years ago (4).

In addition to these intentional omissions, there are, I am sure,

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unintentional ones. This list of methods of treatment makes no pretensions to completeness. It consists of those which seem thoroughly established, or of which I have had personal successful experience. An attempt has been made to give credit only for broad innovations, but I am quite aware that the story might have been written with an entirely different set of heroes. It is the theme that I particularly wish to bring to your attention.

The treatment of pain—To return to more strictly neurologic subjects: it is perhaps natural that *pain* should be the symptom of disease of nervous tissue which earliest demanded and first received specific relief. The use of opium dates back to prehistoric days, and no real substitute for it has ever been found. According to Létiévant (5), the first recorded nerve section for neuralgia was performed by Maréchal, the Court Surgeon of Louis Fourteenth. I have not been able to find any particulars. Létiévant himself, writing in 1872 was familiar with section of branches of the trigeminal, the intercostals, the occipitals, and the sciatic nerves. Peripheral neurectomies have, however, largely fallen out of use, except in the treatment of supraorbital neuralgia, of thromboangiitis obliterans (6), and of tuberculosis of the larynx.

A more refined procedure is intraspinal section of spinal posterior roots first suggested by Charles Dana and carried out by Robert Abbe of New York in 1888 (7). This obviously has the advantage that motor power is preserved. It paved the way for that triumph of surgery, the radical cure of trigeminal neuralgia. Rose (8) was the pioneer in removal of the gasserian ganglion, but his approach has been abandoned. Horsley (9) cut the posterior root by a method resembling the modern one in 1891, but his patient died. Successful results from a practical procedure were announced by Krause (10) in 1893.

A bold step forward in neurologic treatment was suggested by Schüller in 1910 (11) and carried out by Spiller and Martin in 1911 (12): the section of the pathways for pain in the spinal cord. Aside from the practical value of the operation, which has now become a common and standard one, this step opened what promises to be an important epoch in neurology: that of operative interference with structures of the central nervous system for the purpose of altering its physiology.

Except for operations on the sympathetic nervous system, which will be mentioned briefly below, the only new procedure for the

relief of pain which has found wide acceptance is that introduced in 1931 by Dogliotti (13); namely, the subarachnoid injection of absolute alcohol. The method was first used in this country at the Neurological Unit, as far as I am aware, and the staff has convinced itself that the method has definite, though restricted, value. It is a conservative method of treating mild chronic pain; for severer conditions, chordotomy saves time, pain, uncertainty, and the patient's motor power. A field of usefulness for Dogliotti's procedure which deserves further study is in the treatment of certain forms of spasticity.

The surgery of tumors of the nervous system—The first successful operation for tumor of the brain (by Godlee) was recorded in 1884 (14). A tumor of the spinal cord was removed in 1888 by Horsley (15). Annandale (16) reported recovery after operation on an acoustic neuroma in 1893. Successful radiotherapy of a pituitary adenoma was reported by Béclère in 1909. Nordentoft announced successful treatment of gliomas in 1917 (18). From these hesitating beginnings, the surgery of tumors of the brain and spinal cord has made enormous strides, perhaps most strikingly signalized by Cushing's review of his two thousand verified tumors in 1932 (19). I shall make no attempt to trace the steps of the progress, but I should like to point out that it was largely due to the successes of tumor surgery that hopes of successful forms of treatment in other departments of neurology were aroused.

The treatment of convulsions—Epilepsy was recognized as a disease, and treated in prehistoric times. While scattered "cures" have followed the use of any one of a thousand different remedies, only a few measures have become accepted in modern practice. One of these is the use of bromides. This was apparently first recommended by Sir Charles Locock in 1857, in the course of a discussion of a paper by Sieveling (20). Locock's reasoning was simple; an unnamed German had tried potassium bromide on himself, and found it an anaphrodisiac; it was well known that many cases of epilepsy were caused by onanism; he tried it in fourteen cases, and it worked in all but one. It is still recognized as a moderately successful anticonvulsant.

A rational operative treatment for focal epilepsy was reported by Horsley in 1887 (21), namely, excision of an irritable focus of the cortex. The procedure could scarcely be termed an accepted one until after the careful studies of Foerster and Penfield (22).

It appears probable that the more precise information which can now be obtained by electroencephalography will be of particular value in selecting cases for this treatment (23).

On the whole, the most successful treatment for the majority of patients suffering from convulsions of unknown origin is the use of phenobarbital, which was recommended for this purpose by Hauptmann in 1912 (24). It is applicable to a far larger proportion of cases than is surgery, and has a greater anticonvulsant effect in proportion to its soporific effect than bromides or than any of the other barbiturates.

The treatment of epilepsy by ketosis was reported by Wilder in 1921 (25). It is a measure which still finds use in some cases, particularly in petit mal in children.

The drugs at present in use for the treatment of convulsions were all primarily introduced as hypnotics, and the discovery of their anticonvulsant effect has been rather accidental. A systematic search for anticonvulsants by an experimental method was begun at the Neurological Unit in 1937 (26, 27, 28) and is still continuing. It has already yielded one compound, diphenyl hydantoin, which appears to be more effective than phenobarbital, and without appreciable soporific effect. The study of convulsions by means of electroencephalography (23) suggests that there are several types, each due to a distinct physiological mechanism, and possibly each will require individual study and treatment.

Treatment of neurosyphilis—The recognition of syphilis of the nervous system is a relatively modern feat. It was doubtless treated with mercury even before it was recognized. According to Garrison (29), the identity of the man who first introduced mercury into therapeutics is unknown. It is probable that, as far as neurosyphilis at least is concerned, its reign is almost over.

The story of the introduction of salvarsan by Ehrlich in 1910 is familiar to all (30). It is unique in history—a new conception, systematically and patiently pursued by a great genius over many years, and finally a magnificent success, to be compared only with vaccination in its significance to the human race. As a treatment for parenchymatous neurosyphilis, it has largely been replaced by a modification—tryparsamide—prepared by Jacobs and Heidelberger of the Rockefeller Institute in 1917 (31), which did not come into use, however, until 1921 (32). The use of fever in the treatment of neurosyphilis has a long history in the life of one

man. Wagner von Jauregg apparently first noticed its effect in dementia paralytica in 1887 (33), but he dropped the subject, and only returned to it during the War. His first brief paper specifically recommending the use of malaria was published in 1918 (34). Since then, the method has become a standard one.

A few years later, the use of bismuth was proposed by Sazerac and Levaditi (35). The salts of this metal have largely taken the place of those of mercury.

At the turn of the century, there was no known method of treatment of syphilis which would prevent infection of the nervous system. Up to the close of the War, once neurosyphilis was established, there was little hope of arresting its course. At present, the majority of early cases can be cured.

The treatment of other infections—Among infections of the nervous system, brain abscess presents a problem of which the solution is obvious but difficult to attain. Successful operation on an abscess was reported by Morand in 1768 (36). The principles governing operative treatment are gaining slow recognition, and there has been a gradual decline in the average operative mortality.

The next progress in controlling infections came with the rapid growth of bacteriology and immunology in the last quarter of the last century. The Pasteur prophylaxis against rabies (37) in 1885, and the antitoxin against tetanus developed by von Behring in 1892 (38) are now so successful that we can scarcely reconstruct for ourselves the days when those terrible diseases were common.

Meningitis, next to syphilis the most common form of infection of the nervous system, still retains a high rate of mortality. The value of lumbar puncture in its treatment (39) is not yet fully recognized. A specific antiserum against injections with the meningococcus was introduced by Jochmann (40) in 1906. Although widely used, its value is still in some doubt. In the last two years, synthetic drugs of the type of sulphanilamide (Domagk, 1935, (41)) have become a standard treatment, which is amazingly effective, not only against infections by the meningococcus, but against other pyogenic infections.

There is no accepted treatment for, or prophylaxis against, poliomyelitis, encephalitis and herpes. It has been shown that many types of "encephalitis" are in reality not infections of the brain (42). Severe chorea of the Sydenham type, and also that occurring in pregnancy, may be effectively treated by induced

fever (43). The severe neuralgia which sometimes follows herpes usually yields to x-ray treatment (44).

Treatment of deficiency diseases—An increasing number of diseases of the nervous system are now being recognized as due to vitamin deficiency. The first of these was pellagra (45), the treatment of which has now been placed on a sound basis (46, 47). Modern vitaminology may be said to have begun with Eijkman's experiments on beriberi (48). He would have been surprised, perhaps, to see most polyneuritis regarded as subvarieties of beriberi (49), including the type described by Landry (50).

Owing to the recognition that combined system disease of the spinal cord is related to pernicious anemia, it is obvious that Minot and Murphy's discovery of the liver diet for the treatment of the latter should be applied to the former also. There have been disappointing results with liver treatment in some hands, but convincing evidence has been offered that arrest of progress of cord degeneration is the rule, and improvement is common, if large enough doses are used—far larger than needed to control the blood picture (51).

Not only alcoholic polyneuritis (52), but also the characteristic confabulatory psychosis often associated with it, appears to be due in part to a vitamin deficiency (53). It is likely that the same is true of Wernicke's alcoholic polioencephalitis (54). How effective treatment of these conditions will be, remains to be seen.

Treatment of diseases of the sympathetic system—Surgery of the sympathetic nervous system has its beginnings in the last century, but its real successes have come only since the War. It is of definite value in the treatment of Raynaud's disease (Royle, 1918 (55)), and Hirschsprung's disease (Wade and Royle (56)). There have been many disappointments in the treatment of angina pectoris, but alcohol injection of the intercostal nerves as carried out by Mandl (57 appears to be a reliable method of cure of the pain. Certain obscure painful conditions of the extremities are sometimes benefited by sympathectomy (58). Further information should be sought in one of the recent treatises on the subject (3).

A recent accession to the list of conditions amenable to surgery is the carotid sinus syndrome. The clinical importance of the condition has been pointed out by Weiss (59), and the possibility of its surgical relief has been demonstrated at the Boston City Hospital.

Whether or not migraine should be included among surgical diseases is open to question. Cervical sympathectomy (60), alcohol injection of the gasserian ganglion (61), section of the temporal artery and of the meningeal artery (62) have all been followed by success in some instances, failure in others. A remarkable medical treatment for individual attacks of migraine is the use of ergotamine tartrate (63, 64).

Treatment of paralysis agitans and athetosis—One of the most familiar diseases of the nervous system is paralysis agitans. The only accepted treatment for this often distressing condition is the use of drugs of the atropine series, apparently first suggested by Charcot (65). Enormous doses are sometimes tolerated, but often ineffective. Recently, the use of a fresh, hot decoction in white wine has found wide and apparently successful use in Italy. Some of my patients have told me that moderate doses of alcohol, alone or with hyoscine, are valuable. The asthenia which often accompanies the disease may sometimes be relieved in the post-encephalitic type of paralysis agitans by administration of benzedrine sulphate (66), which is also a fairly reliable remedy for the oculogyric crises which accompany it.

In extremely severe unilateral cases, the resort to surgery may be justified. Bucy (67) has recently demonstrated that the tremor may be abolished by an extensive resection of the motor cortex—a possibility vaguely foreshadowed by Parkinson himself (68). At the Neurological Unit, a similar result has been obtained by section of the pyramidal tract in the spinal cord, which impairs the function of the corresponding limbs to an astonishingly slight extent (69).

The somewhat rarer but often far more distressing condition of athetosis has received less attention than it deserves. The first successful attempt at its relief was reported in 1909 by Horsley (70), and his method has been further developed by Bucy and his associates (71). The method first used at the Neurological Unit in 1931 accomplishes the same object by section of the extrapyramidal tracts in the spinal cord (72). It can be used in bilateral cases (best in two stages) and does not destroy the use of the extremities.

A promising start in the medical treatment of athetosis has been made by West (73). He has shown that the intravenous administration of curare will depress abnormal movements over several

days, and this we have been able to confirm at the Neurological Unit (74). Obviously, the method is not suitable for general use at present, but a search for more practical drugs is under way.

The most successful treatment for spasmodic torticollis is the operation devised by Dandy (75).

The treatment of hydrocephalus—The importance of hydrocephalus as a disease has been underestimated. According to Murphy (76), it occurs in the proportion of over 1.5 to every 1,000 "white" births, that is, there are probably two or three thousand hydrocephalic infants born every year in this country. Most hydrocephalic infants are mentally defective from the outset and these are doomed in any case. Many of them, however,—perhaps one quarter—are apparently capable of growing up normally if the pressure can be relieved. There have been isolated successes from various types of operations (reviewed by Davidoff (77)), but only recently have technical improvements permitted a series large enough for statistical purposes to be accumulated (78). In selected cases, the operative mortality may be as low as ten per cent after bipolar coagulation of the choroid plexuses. When hydrocephalus and spina bifida coexist, an alternative method of relief has been successful in a few instances, namely, resection of the abnormal mass of tissue which apparently blocks the circulation of fluid (Parker and McConnell (79) and D'Errico (80)).

Treatment of syringomyelia—Syringomyelia is a hereditary malformation which often exists without giving rise to symptoms. About sixty per cent of cases are improved by persistent treatment with x-rays (Raymond, (81, 82)). In cases resistant to radiation and especially those in which there is pain or a subarachnoid block, operative drainage of the syrinx may afford some relief. This operation was first recorded by Elsberg (83), and was applied in a systematic fashion and recommended by Puusepp (84) of Esthonia, where the condition is apparently far more common than in this country.

Treatment of Méniere's syndrome—A method of treatment of recurrent attacks of vertigo, by destruction of the labyrinths was suggested by Lake in 1904 (85). The operation of section of the auditory nerve was first carried out by Frazier in 1910 (86). Both types of procedure were long neglected, and are only recently coming into their rightful places (87, 88). In addition to the modern operations, medical treatment which is often effective has been proposed by Furstenberg (89).

New medical remedies for miscellaneous diseases—*Narcolepsy* is a disease which is often overlooked or untreated. The overpowering drowsiness which characterizes it is satisfactorily combated by benzedrine sulphate, for which the patients often have a high tolerance (90). Since the introduction of the drug for this purpose, it has been widely used in the treatment of asthenia, fatigue and debility of many types (91)—perhaps too widely, for it is not a drug for indiscriminate use.

An effective treatment for *myasthenia gravis* was found by Mary Walker (92) in 1935, namely, prostigmin, a synthetic substitute for physostigmin (93). *Myotonia*, a disease which is in many ways the opposite of myasthenia—both are apparently disorders of the chemical transmission of the nerve impulse—was relieved by the use of quinine by Kennedy and Wolf in 1936 (94).

Two mechanical substitutes for nervous functions—There are many disease states which produce a temporary cessation of respiration, but are not necessarily fatal otherwise. A respirator was designed by Drinker (95) in 1929, primarily for use in resuscitation from asphyxia and electric shock. It is, however, finding a larger and constantly expanding use in the treatment of poliomyelitis, polyneuritis, and injuries to the spinal cord. A respirator should be part of the equipment of every neurologic service.

Many deaths have resulted from infection of the bladder and kidneys following disease of the spinal cord. A practical device for preventing cystitis was devised by Laver and perfected by Munro in 1934 (96), namely, a tidal drainage apparatus on the principles of a Tantalus syphon. The importance of the apparatus extends far beyond the comfort of the patient and saving in bed linen. The prevention of infection permits a degree of recovery of damaged nerve tissue which would never be possible otherwise. It is simple and inexpensive, and should be available in every hospital.

The prospect of further advances—Since the War, and especially during the past ten years, something of a revolution has taken place in the field of clinical neurology. From a static branch of medicine, with the ideal of predicting irreversible structural changes from rigidly classified syndromes, it has become more dynamic by advancing in two directions. One is toward an interpretation of the activities of an injured nervous system in terms of neurophysiology, and thence toward remedying the defect. Examples of this type of analysis and systematic attempts at

applications of physiologic knowledge are the recent steps forward in the treatment of epilepsy, paralysis agitans and athetosis, and longer strides in the same directions are unquestionably in prospect.

Another type of dynamic concept which is relatively new in neurology is an analysis of the mechanism and pathogenesis of diseases of the nervous system. The gross and microscopic appearance of the brain and cord in practically all of the diseases which we know today was described before the turn of the century. The stages in breakdown of various tissue elements have been thoroughly studied. Attention is now centered on the steps *preceding* irreparable damage. Arteriosclerosis and neurosyphilis were probably the first diseases in which attempts at dynamic interpretation were made, and are still continuing. The mechanism and pathogenesis of multiple sclerosis are now fairly clear (42), and the direction in which an effective treatment is to be sought is beginning to appear (97). Similar advances in the pathology of the deficiency diseases (54), progressive muscular atrophy (98) and amyotrophic lateral sclerosis (98), are in progress, and in the course of time will certainly bear fruit.

Our practical understanding and treatment of nervous and mental diseases is still in an expanding stage. The subject grows more complicated with each year that passes, and while there is a proper tendency for diseases formerly considered to lie within the jurisdiction of the neurologist to pass into the hands of internists and general surgeons—for example tetany and hyperthyroidism—the specialized knowledge and interest of trained neurologists provided with adequate and independent facilities for research, is essential for real progress in the comprehension of many obscure and intricate problems. To reduce clinical neurology to a subdepartment is to subordinate the welfare of patients suffering from diseases of the nervous system.

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VARIATION IN THE CHOLESTEROL, BILE PIGMENT AND CALCIUM CARBONATE CONTENT OF GALL-STONES WITH THE SITE OF STONE FORMATION AND THE DEGREE OF ASSOCIATED OBSTRUCTION*

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The fundamental cause of gallstone formation is still very little understood despite the amount of study which has been devoted to the physiology and chemistry of the bile, the composition of the stones and the associated pathology and bacteriology of the biliary tract.

Stones may form in the gall-bladder or in the bile ducts, and both sites have to be considered in determining the role which any factor may play in the process of stone formation. This fact has often been lost sight of, and proportionately much more attention has been paid to stone formation in the gall-bladder than in the ducts.

Of the various factors that have been considered or are known to influence stone formation, none is better established than obstruction, although it probably is not the most fundamental one involved. Clinical and operative studies have been made of cholelithiasis and of traumatic strictures of the ducts, and analyses have been made of stones removed surgically from gall-bladders and from common or hepatic ducts in an endeavor to throw light on their chemical composition as influenced by obstruction and also on the source of the chemicals themselves, i.e., whether they are derived from the bile or from the wall of the gall-bladder.

The chief building materials of stones in the gall-bladder are cholesterol, bile pigments and calcium carbonate. They become enmeshed in a colloidal ground substance as is common to all concrement formation. They vary greatly in composition from pure cholesterol and pure calcium carbonate stones to almost any mixture of any two or all three of these substances. Pure pigment stones of any magnitude probably do not develop in the gall-bladder.

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Since the work of Aschoff it has been widely accepted that pure cholesterol stones may form in the gall-bladder free from infection but in the presence of stasis, which from the nature of things is not of high degree. Whether or not Aschoff thinks there is an associated cholesterol diathesis is a more debated point. The fact that an otherwise uncomplicated gall-bladder containing pure cholesterol stones is usually visualized after dye administration is proof that if any obstruction is present it is usually of low grade. Little or no pathological changes are found in such gall-bladders.

In contrast, pure calcium carbonate stones are now known to form in gall-bladders and the seat of mild chronic inflammation with either very high degree or usually complete obstruction of the cystic duct by calculi. In all cases to be reported the gall-bladder failed to visualize with the dye. Lantern slide demonstrations were made of one case of solitary cholesterol stone obstruction of the cystic duct with a large calcium carbonate stone that had been observed roentgenographically to grow in the gall-bladder, and of another of multiple cholesterol pigment stones in the gall-bladder with one of the herd obstructing the cystic duct and a large mass of calcium carbonate deposited secondarily in the gall-bladder.

Separate calcium carbonate deposits in the form of a stone, paste or sand were found in 23 of 510 cases of operatively removed gall-bladders. In all 23 cases the cystic duct was obstructed. The source of the calcium carbonate in these cases is the wall of the gall-bladder since the bile is excluded by the obstruction.

Between the pure cholesterol stone on the one hand which develops in the gall-bladder in the presence of stasis with little pathological change, and the pure calcium carbonate stone on the other which forms only if there is very high grade or complete obstruction, are the great group of mixed stones developing usually in herds and in a pathological gall-bladder the cause of which is disputed but which Naunyn and Aschoff have considered as infectious. There is a fairly definite relationship between their contents of bile pigments, calcium carbonate and cholesterol and the degree of associated obstruction of the outlet. There may be fluctuation in the amount of obstruction either from stone or from inflammation and in the amount of pathology in the gall-bladder as a result of which the composition of the different layers deposited on the stones varies accordingly.

In general it may be stated that as stasis increases in inflamed gall-bladders the seat of calculi, whether single or multiple, any deposit which may be precipitated on them shows a tendency to increase in calcium carbonate content; and the same holds true for pigment content up to a certain point beyond which the source of pigment supply is too markedly reduced. Such secondary deposits are darker in color and cast ring shadows in roentgenograms. That they may be laid down during periods of high grade obstruction of the cystic duct by stone is illustrated by the following case: Cholecystography showed 8 radio-opaque ring shadows in the region of the gall-bladder and nonvisualization by the dye. At operation a stone was found tightly engaged in the cystic duct which was excised with the gall-bladder. A roentgenogram showed it to cast a radiolucent shadow, while the 8 stones in the gall-bladder cast radioopaque ring shadows and there was a small amount of separate radio-opaque substance in the fundus. On opening the gall-bladder a yellow, soft stone was found in the cystic duct and 8 hard dark coated stones and a mass of free calcium carbonate in the gall-bladder.

What happened was that 9 cholesterol-pigment stones formed in the gall-bladder; one entered the cystic duct, calcium carbonate began to be precipitated in the gall-bladder but with some bile still entering. A layer rich in calcium carbonate and pigment was then deposited on the stones in the gall-bladder and some free calcium carbonate was also thrown down. The stone in the cystic duct, being more freely bathed in unobstructed bile, remained free from deposit. That the calcium came from the wall of the gall-bladder is supported by the presence of a separate deposit which indicates that at some period the duct was completely obstructed. In other cases a period of inflammatory obstruction may have the same effect. That this is a factor is supported by the cholecystographic finding that stones casting radio-opaque shadows are usually in gall-bladders which fail to visualize with the dye as reported by Graham, and Phemister, Rewbridge and Rudysill.

Further proof of the importance of obstruction in the causation of secondary deposits rich in calcium and pigment is the finding that if gall-bladders are more or less partitioned by a row of stones largely filling them and the outlet becomes incompletely obstructed, calcium and pigment will be deposited on the stones in increasing amounts proceeding from the outlet to the fundus, as

stagnation in the compartments increases, and the cholesterol will be corresponding reduced. Three such cases have been studied by the author.

Since, coming when calcium carbonate is deposited in the presence of complete obstruction of the cystic duct, its source must be the wall of the gall-bladder, and since in incomplete obstruction it is deposited in greater amounts as the obstruction increases, the questions arise if calcium carbonate is deposited in the gall-bladder only in the presence of obstruction and if its source is only from the wall of the gall-bladder.

A roentgenogram was shown of stones found in the gall-bladders of different patients without the presence of stone obstruction of the cystic duct. They contain calcium carbonate variously distributed in nucleus, internal and external layers and even in rays. Gross and chemical analyses show that the calcium carbonate is accompanied by bile pigments and cholesterol in somewhat the same proportions as in the cases of incomplete obstruction by stone just previously reported. The similarity suggests that these layers and nuclei were laid down during periods of temporary obstruction by inflammation or less likely by stones which afterwards passed. That inflammatory obstruction may be sufficiently marked to account for the deposits is shown by the occasional observation of a mucocele of the gall-bladder with complete exclusion of the bile for a long period in the absence of stone in the cystic duct.

Stone Formation in the Bile Ducts

Stone formation in the common and hepatic ducts is usually preceded by stone formation in the gall-bladder and is only set up after one or more gall-bladder stones have lodged in and obstructed the common duct. In this event it may be difficult to determine with certainty which material was laid down in the duct and which in the gall-bladder. Usually there is enough difference in appearance between the deposits laid down in the gall-bladder and in the ducts to make it possible to tell them apart, the gall-bladder stones being richer in cholesterol and often containing calcium. Also the presence of stones in the intra-hepatic radicles makes it certain that they were formed within the ducts. Stones found in the common duct after cholecystectomy unaccompanied by incision and exploration of the duct are usually ones that had

lodged there from the gall-bladder and were overlooked by the operator.

Stones found in the duct after cholecystectomy and choledochotomy with removal of all stones from the duct may be safely considered to have formed there. Studies of such stones reveal that they are very much more uniform in gross appearance and chemical composition than are those formed in the gall-bladder. They are highly pigmented, reddish to brown in color, soft to firm in consistency, and, while there may be lamination, the layers are of almost uniform structure. They may be very numerous and small and in some cases a muddy sand-like material is present. Three such cases have been studied in detail as to chemical composition.

Of the three stone-building substances found in gall-bladder stones, calcium carbonate was absent. Bile pigments and cholesterol were present in large amounts, the cholesterol usually being in excess of the pigments. They demonstrate without a doubt that cholesterol may be precipitated from the bile in the ducts in the absence of the gall-bladder. This finding lends great strength to the view that the cholesterol of stone formed in the gall-bladder may also be derived from the bile.

That obstruction plays a role in setting up stone formation in the ducts is shown by the fact that it is extremely rarely reported as in the intra-hepatic ducts, when the gall-bladder has never been the seat of stone formation. Removal of all calculi from a duct that has been chronically dilated and infected, especially if prolonged drainage is not subsequently carried out, is prone to leave a condition of stasis and infection which leads to recurrence of stones. In nine cases of benign stenosis of the duct following injury at operation stone formation was absent in all and a mud-like material was present only twice.

The following case is illustrative of many of these phenomena:

In 1912 the gall-bladder was opened and a cholesterol stone, which as judged by the coating of calcium on one end had obstructed the ampula with the other end, was removed from the gall-bladder

Gallstone colics recurred and in 1919 he was jaundiced, after which the gall-bladder containing multiple brown stones was removed. Attacks of colic recurred irregularly and at times were accompanied by jaundice. In 1930 he came to our institution and

a large stone was removed from the common duct, the center of which was light in color rich in cholesterol and contained a small amount of calcium. This apparently represented a stone which had migrated from the gall-bladder before the cholecystectomy. On this had been deposited in the duct a dark greenish-brown material of cholesterol and bile pigments.

Five years later because of recurrence of the picture of common duct stones the patient was operated on again and seven large stones consisting of cholesterol and pigment and free from calcium were removed. Nine months later because of symptoms of recurrence his common duct was opened for the third time and a large stone removed, similar in composition to those found at the previous operation and to the peripheral portion of the stone removed at the first operation on the duct.

Résumé

1. There is great variation in the amount of building materials, cholesterol, bile pigments and calcium carbonate, of stones formed in the *gall-bladder*, one cause for which is variation in the amounts of associated obstruction of the cystic duct.

2. Stones in the gall-bladder very rich in cholesterol form when stasis is mild and when associated inflammation is either mild or absent.

3. With increasing obstruction of the cystic duct by stone or inflammation there is an increasing tendency for the gallstone materials laid down to consist of bile pigments and calcium carbonate with a corresponding decrease in the amount of cholesterol.

4. With complete obstruction of the cystic duct (and a mild chronic cholecystilis) pure calcium carbonate may be thrown down in the bile free fluid filling the gall-bladder. The findings suggest that *all* gallstones containing appreciable amounts of calcium carbonate are formed in the gall-bladder and in the presence of some degree of cystic duct obstruction.

5. In marked contrast to stones formed in the gall-bladder, there is relatively little variation in the building materials of gallstones formed in the common duct. They consist of cholesterol and bile pigments in large amounts, calcium being present only in traces.

6. Obstruction is a factor in the initiation of stone formation in the bile ducts as shown by the fact that it is usually set up by the

lodgment of stones which have migrated there from the gall-bladder.

7. These observations would indicate that all gallstones containing appreciable amounts of calcium carbonate are formed in the gall-bladder and that the calcium carbonate is thrown out by the wall of the gall-bladder during obstruction of the cystic duct. As to the source of cholesterol, it can be stated with reasonable certainty that in the case of stones formed in the bile ducts it comes from the bile. The diminishing cholesterol content of stones formed in the gall-bladder with increasing cystic duct obstruction and the absence of cholesterol deposition when the duct is completely occluded and calcium carbonate is being precipitated afford negative evidence in favor of the view that their cholesterol is derived from the bile. These findings do not exclude the possibility that under other circumstances the cholesterol may come from the wall of the gall-bladder.

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